# MICROESSENTIALISM AND REDUCTION
## Can microessentialism explain proteins?

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Tiivistelmä – Referat – Abstract

In discussion on natural kinds one of the central debates is held between monistic and pluralistic view. While monists argue that things are what they are due to their microstructure, pluralists suggest there are several equally legitimate ways to define the nature of a subject. As compounds, proteins raise questions such as "How we should define natural kinds?" and "What makes an object a member of certain kind?" This thesis examines the problems that microstructural monism faces in defining macromolecules and whether it is able to answer the counter arguments.

Recently studies on microbiology have shown that some proteins are able to perform secondary tasks. This ability is called moonlighting and it has raised a need for refining the theories defining proteins. To do so, in this thesis the central problems associated with the functions of proteins are introduced. After this, the solutions offered by the contemporary discussion are considered in order to decide whether microstructural essentialism can survive from challenges set by moonlighting.

This thesis is divided into three sections. The first section (the chapters one, two and three) will introduce the basic terminology, the key concepts, and will provide the frames of the discussion. In the second section (the chapters four and five) the relevant structure and properties of proteins will be examined more closely. In addition to this, the current discussion is introduced in more detail. The section three (the chapters six, seven and eight) weighs various challenges set by functionality and proposes a view according to which microstructuralism may indeed be able to answer these challenges. However, this requires remodeling of the microstructural argument and reviewing its basic assumptions. This is done by reflecting and analyzing writings of Jordan Bartol, William Goodwin and Emma Tobin, with works of Sandra Mitchell, Paul Needham, Jaap van Brakel, Raphael van Riel and Robert Van Gulick.

This thesis concludes that both, microstructuralism and pluralism, have trouble in explaining the structure and dynamic nature of proteins. While pluralism offers a promising ground of explaining the complexity of proteins, it does not emphasize enough the significance of chemical structure. Compared with traditional microstructuralism and pluralism, the views of Jordan Bartol and William Goodwin are in better harmony with current scientific research and, moreover, offer a more appealing answer from the metaphysical point of view. Bartol's view requires adapting dualism of kinds, where macromolecules are classified to chemical and biological kinds. Goodwin is able to hold on to monism by allowing additional levels of explanation. This thesis concludes that Goodwin's theory therefore offers the most promising ground to build a coherent theory of macromolecules. Additionally, Goodwin's levelled microstructuralism is able to retain monism.

Avainsanat – Nyckelord – Keywords
natural kinds, philosophy of biology, metaphysics, proteins, macromolecules, philosophy of science, monism, pluralism

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Tiivistelmä – Referat – Abstract

Nykyisessä luonnollisia luokkia koskevassa keskustelussa keskeinen kysymys on ollut tulisiko luokittelussa omaksua monistinen vai pluralistinen näkökulma. Siinä missä monistit määrittelevät mikrorakenteen olevan luonnollisten luokkien määrittävä tekijä, pluralistien mukaan olennot voidaan määritellä usealla yhtä pätevällä tavalla. Viimeaikaiset tutkimukset mikrobiologian saralla ovat paljastaneet joidenkin proteiinien olevan kykeneviä toteuttamaan toissijaisia toimintoja perustoimintojensa lisäksi. Tätä kykyä nimitetään termillä ”moonlighting”. Tämä ominaisuus on osoittanut tarpeelliseksi proteiineja koskevan määrittelyn, minkä lisäksi se on koettu ongelmalliseksi etenkin mikrostrukturaalisen essentialismin kannalta. Tämä tutkielma tarkastelee niitä ongelmia, joita mikrostrukturaalinen monismi kohtaa makromolekyylien määrittelyssä sekä sitä, onko mikrostrukturaalinen monismi kykenevä vastaamaan sitä kohtaan esitettyihin vasta-argumentteihin.

Tutkielma on jaettu kolmeen osioon. Ensimmäinen osa esittelee keskeisen terminologian ja keskustelun puitteet. Toisessa osiossa proteiinien erityisominaisuuksia tarkastellaan lähemmin ja niiden asema luonnollisia luokkia koskevassa keskustelussa nostetaan keskeisen tarkastelun kohteeksi. Kolmannessa osiossa proteiinien asemaa koskevan nykykeskustelun eri teorioita arvioidaan tarkoituksena selvittää, onko proteiinit mahdollista määritellä mikrostrukturaaliseen essentialismiin nojautuen. Tämän arvioinnin perusteella voidaan todeta, että mikrostrukturaalinen teoria on kykenevä vastaamaan sitä kohtaan esitettyyn kritiikkiin, mutta tämä vaatii teorian uudelleen muotoilua ja taustaoletusten tarkempaa tarkastelua. Työn keskeisinä lähteinä toimivat erityisesti Jordan Bartolin, William Goodwinin, Emma Tobinin sekä Sandra Mitchellin, Paul Needhamin, Jaap van Brakelin, Raphael van Rielin ja Robert Van Gulickin luonnollisia luokkia koskevat tekstit.

Tämä tutkielma esittää, että monismi perinteisessä muodossaan on liian jyrkkä kanta kuvaamaan makromolekyylejä. Toisaalta pluralismi ei anna tarpeeksi painoarvoa kemiallisen rakenteen merkitykselle. Pluralismin sijasta Jordan Bartolin ja William Goodwinin esittämät näkemykset ovat paremmin yhteen sovitettavissa kemian- ja biotieteiden näkemysten kanssa. Tämän lisäksi heidän teoriansa kykenevät vastaamaan myös metafyysisten kysymysten haasteisiin. Bartolin näkemyksen mukaan makromolekyylien suhteen tulisi omaksua dualismi, jossa makromolekyylit luokitellaan kuuluviksi sekä kemialliseen että biologiseen luokkaan. Goodwin sen sijaan kykenee säilyttämään monismin sallimalla vaihtoehtoiset tulkintatasot, joista huolimatta keskeinen määrittävä tekijä on makromolekyylin mikrorakenne. Verrattuna tiukkaan monismiin ja pluralismiin Bartolin ja Goodwinin teoriat kykenevät paremmin ymmärtämään proteiinien dynaamista luonnetta. Mikrostrukturaalinen monismi on Goodwinin teorian muodossa kykenevä vastaamaan sitä kohtaan esitettyihin vasta-argumentteihin. Siten, mikäli halutaan omaksua monistinen kanta, Goodwinin teoria kykenee tarjoamaan parhaat lähtökohdat makromolekyylien luokitteluun.

Avainsanat – Nyckelord – Keywords
luonnolliset luokat, metafysiikka, proteiinit, biologian filosofia, makromolekyylit, tieteen filosofia, monismi, pluralismi

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# 1 Introduction

Natural kinds have been one of the central subjects of philosophy of science since Kripke (1980) and Putnam (1975) introduced their studies in the middle of the 20th century. As biological knowledge has increased they have become one of the most studied subjects of natural kind discussion. In the philosophy of chemistry compounds and macromolecules have become a central part of the natural kind studies and much of the debate has been on whether the properties of elements and compounds may be reduced to their microstructure (or chemical structure) or not (Bird & Tobin, 2017).

As compounds, proteins raise questions such as “How we should define natural kinds?” and “What makes an object a member of certain kind?” Different theories on natural kinds have tried to explain them. In this thesis monism is defined in the following way:

Monism = The nature of a subject is reducible to a single source.

Depending on the monistic theory and philosophical context this primary source may vary. However, in the discussion on natural kinds, the monism usually means microstructuralism.

Microstructuralism = Things are what they are due to their microstructure, which is usually (but not necessarily) understood as their chemical structure.

Many philosophers (see for example Havstad, 2017) find compounds problematic for the microstructural theory as compounds do not seem to fit well with the monistic demands of structural similarity. For example, recent developments in microbiology have revealed that protein’s functions are dependable on its surroundings; that is other molecules, tissues and biological environment. Therefore, it appears microstructuralism is overlooking some important aspects of how proteins may be defined.

Pluralism = there are multiple, equally legitimate, ways to categorize a subject.

Therefore, for pluralist the nature of a subject cannot be reduced to one primary source. As microstructuralism has faced problems with functionally variable subjects, pluralists have suggested this should be taken as an argument in favour of adopting pluralism instead (see Bartol, 2016; Slater, 2009). While microstructuralists, alongside other monists, consider the microstructure to be what determines the identity of a thing, pluralists claim the essence cannot be described merely by microstructural properties. For example, proteins interact with their surroundings and therefore in vitro research is able to reveal only small parts of the functional capability (Mitchell & Gronenborn, 2017, p. 717) Furthermore, pluralists have suggested that examples provided by recent research on moonlighting proteins prove that the microstructural theory cannot characterize the essence of macromolecules in a satisfactory manner. In addition to microstructuralism and pluralism, some philosophers have tried to establish middle-ground either by revisiting microstructuralism or by narrowing down pluralism toward a less permissive form (see Bartol, 2016; Goodwin, 2011). For example, recently William Goodwin (2011), has offered his own version of microstructuralism, that is trying to answer to the counter arguments and to update the theory to meet the challenges.

Recently studies on microbiology have shown that some proteins are able to perform secondary tasks. These *moonlighting* proteins have raised much interest in the philosophy of chemistry, as the current descriptions of chemical kinds have faced problems in explaining them. In this thesis I will view central problems associated with the functions of proteins and weigh some of the solutions offered by the contemporary discussion on the subject. To decide whether microstructural essentialism can survive from challenges set by moonlighting and whether remodeling of the theory is needed, it is also essential to view the roots of the discussion on macromolecules. Underlying assumptions and premises are important to recognize especially when we are faced with new findings that the current theories face troubles in explaining.

This thesis is divided into three sections. The first section (the chapters one, two and three) will introduce the basic terminology, the key-concepts, and will provide the frames of the discussion. As a branch of philosophical study, natural kinds are somewhat recent and have been an interest of philosophical study from the late 19th century. Although the questions set have their roots in antique and classical philosophy, this thesis concentrates on more recent background, which offers more meaningful discussion and argumentation for the subject of the thesis.

In the second section (the chapters four and five) I will introduce the relevant structure and properties of proteins. Additionally, I will introduce the current discussion more closely by examining the contemporary research on the subject. The second section concentrates on central philosophical problems related to macromolecules and especially to proteins. To that end, I will examine the most common counter arguments against microstructuralism as well as some answers to them provided by recent philosophical studies.

In the section three (the chapters six, seven and eight) I will weigh challenges set by functionality and propose a view according to which microstructuralism may indeed be able to answer these challenges, but it requires remodeling the thesis and reviewing its basic assumptions. On this I lean strongly on Emma Tobin's, Jordan Bartol's and William Goodwin's views (Bartol, 2016; Goodwin, 2011; Tobin, 2010a, 2010b). While Tobin is skeptical about microstructuralism and more sympathetic towards pluralism, I claim Goodwin's monism is in better harmony with current scientific research and offers a more appealing answer also from the metaphysical point of view. In her paper "Microstructuralism and macromolecules: the case of moonlighting proteins" (2010a) Tobin considers some of the central counter arguments against microstructuralism. Tobin suggests that while microstructuralism is able to answer to most of the arguments raised against it, the case of moonlighting proteins is problematic for both stronger and weaker forms of microstructuralism (ibid.). It is notable that while some philosophers

have found macromolecules problematic for the stronger versions of microstructuralism (see for example Hendry, 2009 and Needham, 2011) Tobin considers it well-equipped to answer the problem (Tobin, 2010a).

Mitchell and Gronenborn, as well as Havstad, have established their own arguments against microstructuralism (Havstad, 2017; Mitchell & Gronenborn, 2017). Mitchell and Gronenborn support pluralism, as monism, in their view, is unable to take into account the functional aspects of proteins (Mitchell & Gronenborn, 2017). Havstad is more positive towards microstructuralism, but admits it struggles answering many essential questions related to chemical and biological kinds (Havstad, 2017).

After examining counter arguments against microstructuralism, I will examine more closely William Goodwin's (2011) view of remodeled microstructuralism. According to Goodwin, microstructuralism is able to explain proteins and their functions. However, this requires that the functional aspects of proteins are taken into account and not straightforwardly reduced into the microstructure. Goodwin does not suggest we should jettison monism for the sake of pluralism: he proposes a view according to which there are, in addition to microstructural properties, in fact, other ways to classify natural kinds. These additional levels should be taken into account in the taxonomical practice. Goodwin claims that accepting these additional levels does not mean accepting pluralism. Supplemental levels[1] are *additional* while the foundation itself remains microstructural. Goodwin suggests multiple levels are needed in order to understand the complexity of proteins and adding additional levels should not be viewed as contradictory to microstructuralism. Instead they are one of the most promising ways of explaining functionally diverse macromolecules. Adding additional levels enables us

[1] Additional ways of categorizing, that may vary depending on the situation.

to build coherent arguments about proteins as natural kinds, without leaving their essential properties out. (Goodwin, 2011.)

This thesis concludes that while pluralism offers a promising way of explaining the complexity of proteins, it does not emphasize enough the significance of chemical structure compared to the other properties (such as function) of substances. Therefore, though pluralism might be methodologically purposeful, it misses substantial explanatory power. Moreover, while there are problems associated with microstructuralism, it does not follow from this that pluralism would succeed better in explaining macromolecules, such as proteins. It is obvious that all the current theories have faced some difficulties in explaining macromolecules. Yet, it seems apparent, that some properties are more essential for the identity of macromolecules than others. Therefore, macromolecules seem to have their essential roots in microstructural properties, even if we consider functional roles important for their nature.

# 2 Macromolecules as natural kinds: historical background

Much of the discussion related to the natural kinds, especially in the field of chemistry and macro-biology, is fairly recent. Furthermore, since natural sciences bring all the time new information to the area of studies there are many new promising adaptations of classic theories. Despite of this, or perhaps because of this, it is also essential to understand the roots of the current debate and the grounding theories from where the contemporary views have emerged. Even though there are various, often competing, theories, much of the theory background is shared and this common background is an important part of all the current theories. Moreover, understanding the past enables us

to see why some questions have been regarded as crucial and why these questions have been so hard to answer until now.

In the next chapters I will introduce the main views regarding the ontology of natural kinds. If we adapt the position that there actually are natural kinds that we may talk about, it gives a rise to new questions: what are these natural kinds and from where do they get their identity? Can their essence be reduced to their physical structure or should we categorize substances by several different ways? With the question of whether we ought to adapt monism or pluralism, the study of reduction becomes as an important part of the inquiry. Therefore, the following chapters will introduce some basic claims and theories on natural kinds and their ontological classification. These concepts are examined mostly in the context of macromolecules, but as they also are a part of a wider theory web, some general aspects about the theories on natural kinds are considered.

## 2.1 Theories of natural kinds

The term “Natural kind” has its roots in the work and thought of J.S. Mill published in his work concerning language and logic in 1843 (see Mill, 2002). After Mill, it was developed further on mostly by the works of Saul Kripke (Kripke, 1980) and Hilary Putnam (Putnam, 1975). With that in mind, several philosophers have contributed to the subject and offering different solutions to the questions related to the essence and identity of natural kinds.

### 2.1.1 Realism and nominalism debate

Realism is an ontological view according to which there indeed exist entities called "natural kinds". According to the view "the natural divisions between kinds reflect the boundaries between real entities" (Bird & Tobin, 2017). Should we have a separate class of entities called universals, in order to be able to speak of properties? While the realists think this way, the natural kind nominalists do not share this view. Bird and Tobin state: "There is an analogous debate as regards natural kinds, whether in order to account for our natural kind talk and our natural classifications, we need a special sort of entity in our ontology." (Bird & Tobin, 2017.) According to natural kind nominalism there is no need for any universals for us to have natural classifications: the individual can be classified into kinds without extrapolating any entity beyond the individuals. On the other hand, the realists think we do need an entity "kind" to be able to express the differences between natural and non-natural classifications. Natural kind terms can be described as terms, which enable us to speak of the mind independent actual world. Lately natural kind realism has faced lots of criticism. Nevertheless, it is still widely supported position.

### 2.1.2 One or multiple ways?

One of the key questions, especially in the case of macromolecules, is whether there is a one privileged way to sort natural kinds or multiple different ways which are equally legitimate. Monism and pluralism have both their own ways of understanding the essence of macromolecules (and other natural kinds) and the identity of objects. However, monism and pluralism should not be understood as merely two contradicting extremes. Both lines of understanding have developed many different approaches to classify natural kinds. This makes the discussion of the subject challenging, even though it offers much richer variety of explanatory theories than merely understanding monism

and pluralism as two completing ends. There are many different theories and they often remind each other closely in many parts. Because of this, an integral part of this thesis is to introduce some of the essential divisions with their applications. This enables us to understand some central problems associated with philosophical discussion on natural kinds, as I later proceed to assess the views supported by contemporary philosophers in the context of protein taxonomy.

### 2.1.3 Essentialism and pragmatism

Do natural kinds reflect worldly beings existing in the actual world or are they classifications emerging from the pragmatic decisions we make (see Goodwin, 2011, p. 533)? To an essentialist, natural kinds are mind-independent. There are important key questions related to essentialism. The first question is, is the particular, belonging to a certain kind essentially a part of that kind and does this state of belonging describe an essential property of the particular. The second question is do the kinds themselves have any essential properties. Like Bird and Tobin state: "for each kind K there is some property Φ of the kind such that it is essential to K that Φ(K)" (Bird & Tobin, 2017)

The first one, individual essentialism, might be hard to find appealing without accepting the latter, essentialism about kinds, but the essentialism about kinds does not imply the first. Bird and Tobin provide an example form chemistry to clarify the logical relation between these two:

> "A nucleus of neptunium-239 may undergo beta decay, in which one of its neutrons emits an electron leaving a proton. As a consequence, the nucleus now has one more proton and so is a nucleus of neptunium no longer but is now a nucleus of plutonium. This description is consistent with the claim that it is essential to neptunium that nuclei of neptunium atoms have 93 protons whereas it is essential to plutonium that its nuclei have 94 protons. But one may also claim, as the description implicitly suggests, that one and the same nucleus persists through this transformation. If that is so, then a particular has retained its identity while undergoing a change of kind." (Bird & Tobin, 2017.)

Bird and Tobin emphasize the most essentialists consider the kinship essential to an object, but the example demonstrates it “does not follow immediately from the claim that kinds have essences” (Bird & Tobin, 2017).

## 2.2 Scientific reduction

Concept of reduction is an integral part of the discussion on natural kinds. To what extend the higher lever properties may be reduced to the lower-level, fundamental properties? Can we extrapolate all the higher-level functions and structural properties from the microstructure? And if so, how strong is this reduction? If we argue this is not possible, what kind of relationship occurs between the higher-level and the lower level? How we understand the meaning of causality and reduction depends greatly of the theory we adopt. Especially Ernest Nagel (1961) has studied these questions. While his studies are mostly of reduction in the context of scientific explanation they also bear importance for ontological research. The next chapter looks at some basic views of Nagel.

### 2.2.1 Ernest Nagel

Ernest Nagel’s theories on reduction bear significant meaning to the contemporary discussion over scientific reduction. Raphael van Riel summarizes important aspects of Nagel’s model in following manner:

> “…reduction is (i) an explanation of (ii) theories, which is cashed out in terms of (iii) derivation with (sometimes) (iv) the help of bridge laws. According to these four main features of the official model, there are four

> fields of additional questions that need to be answered to fully characterize the model. Such questions regard (i) reduction as explanation, (ii) the relata of the reduction relation, (iii) derivability, and (iv) the status of bridge laws." (Van Riel, 2011, pp. 355–356.)

Nagel treats reduction as a special kind of explanatory relationship (1961, p.338). An important part of his theory is the concept of bridge principles. Nagel also makes a distinction between arbitrary and non-arbitrary reduction. Raphael van Riel and Robert Van Gulick take this to mean the theories should be consciously chosen and have rational, solid foundations, and the reducing theory "should be better established than the reduced one" (van Riel & Van Gulick, 2016).

In addition to solid foundations, there should be an aspiration to unification, where the reducing theory is able to correct and to add new content to the reduced theory. Nagel's theories have raised much discussion and not all have been willing to accept them. The new wave theorists have found Nagel's bridge principles unsatisfying and claim they do not represent the way we actually use the principles. Instead the new wave theorists argue that the principles are not born the way Nagel claims. Instead they emerge from the discoveries of similarities between the reducing and the reduced theory. (van Riel & Van Gulick, 2016.)

According to van Riel and Van Gulick "Reduction is (i) a kind of explanation relation, which (ii) holds between two theories iff (iii) one of these theories is derivable from the other, (iv) with the help of bridge laws under some conditions." (van Riel & Van Gulick, 2016)

It is important to note Nagel's theory may be understood as an *epistemological* model of reduction instead of an ontological one (van Riel, 2011, p. 356; Sarkar, 1992, p. 17) since it presents a purely explanatory model of reduction. Even if the epistemological reduction implies of the presence of ontological reduction, it is not necessarily so (see

McIntyre, 2007). Nagel's theory is also called *direct reduction* in distinction from *indirect reductions*. While direct reduction explains the reduced theory itself, indirect theory "explains the occurrence of the phenomena of the reduced theory" (van Riel, 2011, p. 356). However, van Riel and Van Gulick point out it seems Nagel himself considered his theory indirect (van Riel & Van Gulick, 2016).

### 2.2.2 Problems in reduction: property identity

The theories of reduction are closely linked to the concepts of identity and similarity. 'A reduces to B' (where 'A' and 'B' are schema letters, which stand for terms that refer to kinds, events, states, individuals, or the like) expresses a truth only if a corresponding statement of the form 'A = B' expresses a truth as well" (Van Riel, 2011, p. 747). As it often is in the case of philosophy, these kinds of theories are by no means as simple as they seem. Van Riel claims that such statements create a problem:

> "Consider the statement 'water reduces to $H_2O$'. According to the interpretation of reduction as being based on identity, this statement expresses a truth only if water is identical to $H_2O$. At the same time, $H_2O$ does not reduce to water (because the reduction relation is asymmetric)! Accordingly, we cannot define this notion of reduction in terms of identity. The reduction relation is asymmetric (and, thus, irreflexive). Identity is not." (van Riel, 2011, p. 748.)

This means A and B need to have properties that differ in some aspect from each other, but those properties seem to be hard to find (van Riel, 2011, p. 748). There are three alternatives for property-identity: supervenience, realization and causation. According to supervenience, the superveniet states are dependent and the state that *supervenes* is above the one *supervened*. However, van Riel and Van Gulick note that this is not enough for reduction. Furthermore, for monist's point of view, supervenience does little good, since it leads to weak dualism. (van Riel & Van Gulick, 2016.)

When discussing of reduction and identity, it is important to make distinction between different types of reduction. While studies on epistemological reduction are interested in scientific practice and how the knowledge on different subjects is actually gained, study of ontological reduction is focused on such questions as *what the relationships of worldly beings are and if they may be reduced to each other, how*. While these different kinds of reductions do bear meaning for the philosophical research of macromolecules and natural kinds, the questions of ontological reduction are more central to the subject of this thesis. For example, in the case of proteins we may ask what the relationship of structure and function is. Can they be reduced to each other some way and if so, how? These questions are the central concern in the Chapter 6, as different kinds of functions of proteins are examined more closely.

## 2.3 Of multiple realization

How should we approach the cases where a protein has an ability to perform different tasks while retaining the same chemical structure? One way to examine these kinds of cases is by reflecting them with theories of *multiple realizability*. While theories concerning multiple realizability of kinds has often been interested of cases, where structurally different compounds share the same function, the theories may also help to enlighten the opposite situations.

Multiple realization is a thesis often used in the context of philosophy of mind. Thesis states that different mental properties may be shared by different kinds of physical kinds (Bickle, 2016). The argument of the thesis is that if physically different kinds share the same realization of some sort, we may claim the higher lever properties are not reductive to the structural properties. For example, if a protein *a* and protein *b*, are both

capable to perform a function Z, we may not reduce the Z to the structural properties of proteins.[2]

As Thomas W. Polger and Lawrence A Shapiro put it, “multiple realization occurs when the same psychological function is performed in different neural ways.” (Polger & Shapiro, 2016, p. 45). When examining whether two individuals belong in the same natural kind, this becomes an essential matter. If two different structures perform the same functions, do they belong in the same kind? Much discussed example of the studies on multiple realization and its conditions is the similarity of an octopus eye and a vertebrate eye. The octopus’s eye has structurally many similarities with a vertebrate eye, and it is able to perform the same tasks. Yet, it does not share the same evolutionary origins as the vertebrate eye. Do the both visual organs still belong into the same kind “eye”?[3]

What is to be asked is whether an octopus eye is similar to a vertebrate eye despite their different background. Or we can consider them as different kind. Whether we adopt the first or the latter position depends largely of how strong emphasis we give on the evolutionary background, the microstructural similarity and the functional similarity. The octopus and the vertebrate eye have analogous structure yet different background. If we consider the evolutionary background as the determining factor, then they are not similar. If we, on the other hand, give more weight to functional and operational similarity, then the two seem to be alike. (Polger & Shapiro, 2016, p. 60.)

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[2] To such as the chemical structure.

[3] It is often relevant to draw a difference between the conventional and the scientific names. For example, we generally speak of bananas as fruits, yet botanically they are berries. Strawberry is commonly referred as a berry, yet scientifically it is an aggregate fruit.

If we consider the octopus eye and the vertebrate eye similar and therefore belonging in the same kind, there is no case of multiple realization. However, if we consider them to be different kinds, yet performing the same function, multiple realization occurs. This means distinction needs to be made between relevant differences and non-relevant differences. Polger and Shapiro clarify this in the following manner. It is true that both, the human eye and the octopus eye are structurally camera eyes. Therefore, they have the same basic mechanism. However, camera eyes are not all alike. There are many different kinds of variations in how the structure is actually gained. These structural differences between camera eyes may be considered as multiple realization. (Polger & Shapiro, 2016, p. 60.)

As it comes to proteins and their ability to moonlight, the case is different. As the moonlighting is an ability of a protein to perform *different tasks with the same structure* it may be viewed as an opposite case for the brain neuron example. However, when several tasks are performed with a single structure, we may say it strongly implies the functions are not necessarily reductive to the structural properties and vice versa. For example, in the case of functions, etiological theory and dispositional theory look for the explanation from historical and teleological aspects. Alongside with these, interaction with surroundings may be considered as significant when explaining functions. Thus, reducing everything to a chemical structure leaves some essential questions unanswered. Ability to perform different functions with a same structure strongly implies chemical structure on its own is not sufficient explanation for a natural kind. We may, of course, claim that even the functional properties are reducible to the chemical structure (see Hendry, 2006). However, this does seem to give only a partial explanation. Moreover, it seems that the ability of performing several functions is itself a significant trait and leaving such out of the explanation wound be ignoring an interesting and significant property for a sake of a seeming simplicity. Therefore, there is a call for more subtle theory than a straightforward reduction.

# 3 Macromolecules: the background of the current discussion

Jordan Bartol (2016), names two central questions related to the classification of macromolecules such as proteins. The first is an epistemic question and the latter metaphysical question. While the former is interested of the different aspects of scientific practice and investigation, the latter examines the questions of more ontological kind. (Bartol, 2016, p. 532.) One of the ontological key questions is whether the macromolecules can be taxonomically grounded to their microstructure. The epistemic question belongs to area of philosophy of science and can be also considered as an interest of ethics of science[4]. That been said, the next chapter concentrates more on the metaphysical question as it forms the central problem in classification of proteins. Moreover, the moonlighting of proteins has brought new information to this problem.

Since biochemical classification has its roots in both, chemistry and biology, it bears elements from both classification structures (Goodwin, 2011, p. 533). It is therefore central to find how the classification of macromolecules that can be can be developed to cover the information provided by these different backgrounds (Goodwin, 2011, p. 534). Whether this should be done by reduction to microstructural properties, by pluralistic approach, or some other method is debatable. Microstructural essentialism has been popular, especially in the philosophy of chemistry, but lately there has been a rising demand for a theory able to solve the problems microstructuralism has faced. On the other hand, those who still favour microstructuralism have searched ways to improve the theory and to fill the explanatory gaps the counter arguments have shown.

While at the area of modern chemistry microstructural essentialism is widely supported, the biological taxonomy has often been regarded as pluralistic and anti-essentialist

[4] As it examines the normative questions related to scientific practice.

(Goodwin, 2011, p. 534). The functional aspects have had more weight among taxonomical identity questions of biology than in the philosophy of chemistry. Perhaps because of this, lately one of the key questions in the philosophy of microbiology has been "revealing how, and on what basis, bio-chemicals are individuated, or sorted into kinds" (Goodwin, 2011, p. 533). While the micro-organisms have been traditionally sorted into kinds by their chemical structure, the new knowledge of their functional capacities and structural fine mechanism have raised a need of refining the theory and arguments. Proteins form one of the most promising subjects for this inquiry, since they hold a unique position as macromolecules with versatile functions. Additionally, they have an un-replaceable, crucial role as a part of organisms and of all living things, and recent biological studies have revealed many new interesting roles they perform (see Tobin, 2009, p. 42). Like all macromolecules, proteins are consisted of elements and therefore offer a promising ground to examine the relation between macromolecules and elements in the context of natural kinds.

The new information about structure and functions of proteins has evoked a question whether we should adopt monism or pluralism in the case of biochemistry and macromolecules (Goodwin, 2011, p. 533). According to microstructuralism, the microstructure alone (or the chemical structure of an element), determines its behavior and identity. Whether the microstructure and the chemical structure should be taken as synonyms, is still debated, but often they are understood as so.

## 3.1 Question of water and $H_2O$

When we consider natural kinds and their essence in the context of chemistry and macromolecules, we soon come across with a debate about the identity of water. As the philosophical problems of the definition of water bear a resemblance to those much discussed in the study of macromolecules, it is useful to take a closer look of these arguments.

On a molecular level a classic case study of essentialism is whether water may be reduced to $H_2O$ or not. This question was first set by Kripke (Kripke, 1980) and Putnam (1975) and it is to be noted their theories were of philosophy of language and mainly semantic arguments. Kripke and Putnam introduced a theory according to which proper names and natural kinds are *rigid designators*, which hold a meaning independent of the speakers (Kripke, 1980; Putnam, 1975). "A rigid designator designates the same object in all possible worlds in which that object exists and never designates anything else"(LaPorte, 2006). The term "water" therefore refers to liquid made of $H_2O$ in all possible worlds. In conclusion, the chemical microstructure is fundamental for water (Bird & Tobin, 2017). While it is important to remember Kripke's and Putnam's arguments are semantic, it is possible to examine the metaphysical questions with them. The examples introduced by Kripke and Putnam may be used for the metaphysical inquiry and *the Kripke-Putnam framework* can be understood as a certain type of approach to Natural Kind Essentialism (Tahko, 2015, p. 800).

Needham strongly criticizes the microstructural view by arguing water cannot be described merely by its compositional formula. According Needham, compositional formula is not a microdescription of a compound but more of a description of proportions and amounts. (Needham, 2011, p. 9.) However, it is not yet unchallengeable that this makes the compositional structure unfit as microdescription.

To further support his view, Needham examines the behavior of water in different conditions. Water has very different microstructure in the gaseous, liquid and solid state, which, according to Needham, makes the description based on merely chemical properties problematic. (Needham, 2011, p. 9.)

Needham and van Brakel suggest water cannot be reduced to its chemical structure without taking into account the properties of the oligomer structure and other factors such as thermodynamic contexts. Hence, it seems many of the properties of water cannot be simply reduced to its chemical structure, $H_2O$. (Bird & Tobin, 2017; Needham, 2000; van Brakel, 2000) However, it may be argued that the structure of $H_2O$ molecule explains its polar behavior, which in turn explains why the molecules have ability to form oligomers (Bird & Tobin, 2017).

Joyce C. Havstad (2017) thinks that along $H_2O$ there are other important chemical requirements for water. Even more, according to her, Hendry has admitted it too. (Havstad, 2017, p. 7) Most of water is in forms of "bodies of water" including also other chemical substances than $H_2O$. For example, dissociated water molecules are important for distinctive functional properties of water (Havstad, 2017, p. 9). Havstad proposes that if liquid water were solely $H_2O$ molecules it would not have the same properties as water has. This same problem can be extended to macromolecules. Havstad finds the mixtures such like concrete problematic for microstructuralism. Concrete is mixture of water, aggregate and cement. However, aggregate covers many different kinds of materials, which leads to instances of chemical kind "concrete" having different chemical structure. (Havstad, 2017, p. 14.) This, of course, implies the chemical structure is not sufficient explanation, unless we are willing to admit the different instances of concrete are not actually of same kind but different sorts of substances, mistakenly classified into same group called "concrete".

To put it another way, if elemental composition is what determines the sameness of chemical substance, concrete does not seem to be one singular substance. Instead, like

Havstad points out, there are as many kinds of concrete as there are examples. (Havstad 2017, p. 14.)

## 3.2 Macromolecules, microstructure and essential questions

According to microstructuralism the decisive role of chemical structure can be extended to compounds (Bird & Tobin, 2017). This means compounds such as macromolecules get their identity from their chemical structure. Does this imply, we should overlook the functional roles macromolecules play and to reduce them solely to their chemical structure? And moreover, can the functional roles be reduced this way without losing essential information about them? Should the functional properties even be considered as significant and meaningful for the question of kindhood and identity? These questions are significant in the context of proteins and their status. Since many philosophers do not agree even of these grounding questions, it is understandable that the consensus of the essential properties of macromolecules, and how they should be categorized, has been hard to reach. What brings its own challenge to this is that biochemists often use different categorizing systems depending on their need. These methodological choices do not necessarily indicate any essential claims, but they might be confused as such. To that end, this suggests, there are some underlying inconsistences: One reason microessential approach has been criticized and found problematic is that proteins seem to have more intricate and versatile properties than microstructuralism seems to suggest.

Bartol (2016, p. 531) has come to the same conclusion by pointing out the chemical kinds have been usually understood timeless and unchanging, while biological kinds have been thought to be more evolving and changing. This may have given a reason to overlook the functional properties that do not fit well with the idea of unchanging identity and a neat structure. But even more, this puts macromolecules, such as

proteins, in an interesting place of an intermediate compositions with somewhat in-between status (Bartol, 2016, p. 531). While proteins can shed new light on classification practice of macromolecules, their study also reveals deeper questions on natural kinds and therefore is meaningful also for overall understanding of natural kinds. However, microstructuralism may be also viewed in less strict sense as the traditional reading suggests. If we agree that microstructuralism does not require strong reduction we may have more room to search satisfactory explanations for molecular structures. Furthermore, softer reading enables us to add additional levels and definitions. Lack of this might have been one reason for the classification problems in philosophy of natural kinds.

# 4 Proteins

To understand the philosophical discussion about proteins it is necessary to take a look of some basic aspects of their biology and chemical structure. Proteins are important part of every living organism and because of their importance their functions and structures vary greatly. However, certain basic structure is present in all different proteins. In the next chapters I will introduce briefly the protein structure and their functional roles. After this I will examine more closely different question and problems related to proteins, their taxonomy, and their status as natural kinds.

## 4.1 Structure and function

Proteins are important part of many activities and functions of organisms. Proteins are formed by amino acids arranged as polymers. Polymers of amino acids are called polypeptides, from which each protein consists by folding and coiling into a three-dimensional conformation. Figure 1 presents the different phases of the protein conformation. An amino acid sequence determines the final shape of a three-dimensional protein and the specific conformation determines how the final protein works. In the structure of a protein, there can be distinguished three levels of structure, which are called *the primary*, *the secondary*, and *the tertiary structure*. If a protein is formed by more than one polypeptide chain (a protein subunit), it has also a fourth structural level called *the quaternary structure*. The monomer subunits of the quaternary structure are attached to each other as illustrated more detailed in Figure 2. Therefore, while some proteins are formed by a singular polypeptide chain, others may have several similar subunits in them. The primary structure of a protein is its amino acid sequence whose structure is determined by the genetic information. Folding and coiling of the polypeptide chains form the secondary structure. This gives the first interpretation of the final form of a protein. The tertiary structure is the overall shape of the polypeptide with bonding interactions between side chains (R groups) of amino

acids. In the case of proteins with more than one protein subunit, the quaternary structure is the overall shape of the protein that results from the arranging and interaction of the subunits, which finally form a larger structure.

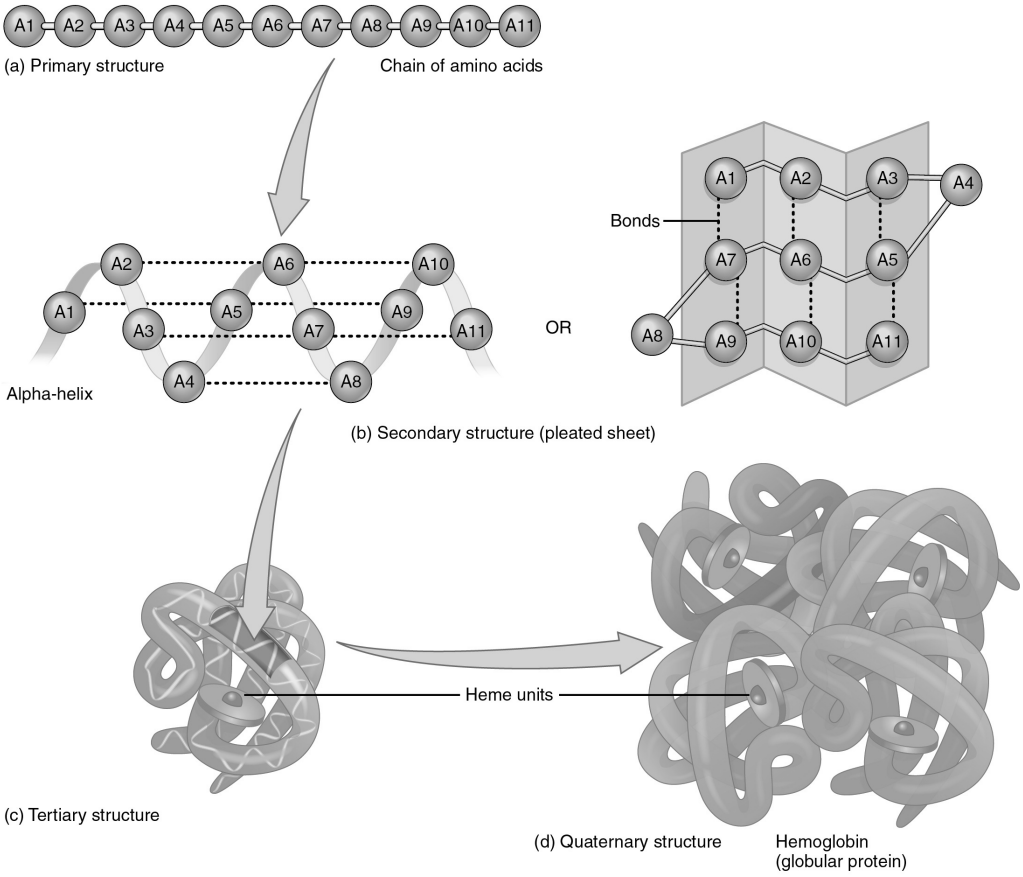


**Figure 1: Different states of protein structure[5]**

[5] OpenStax College - Anatomy & Physiology, Connexions Web site. *File:225 Peptide Bond-01.jpg*, http://cnx.org/content/col11496/1.6/, Jun 19, 2013. Retrieved from https://commons.wikimedia.org/w/index.php?curid=30131163, 2.1.2018. Used under CC BY 3.0.

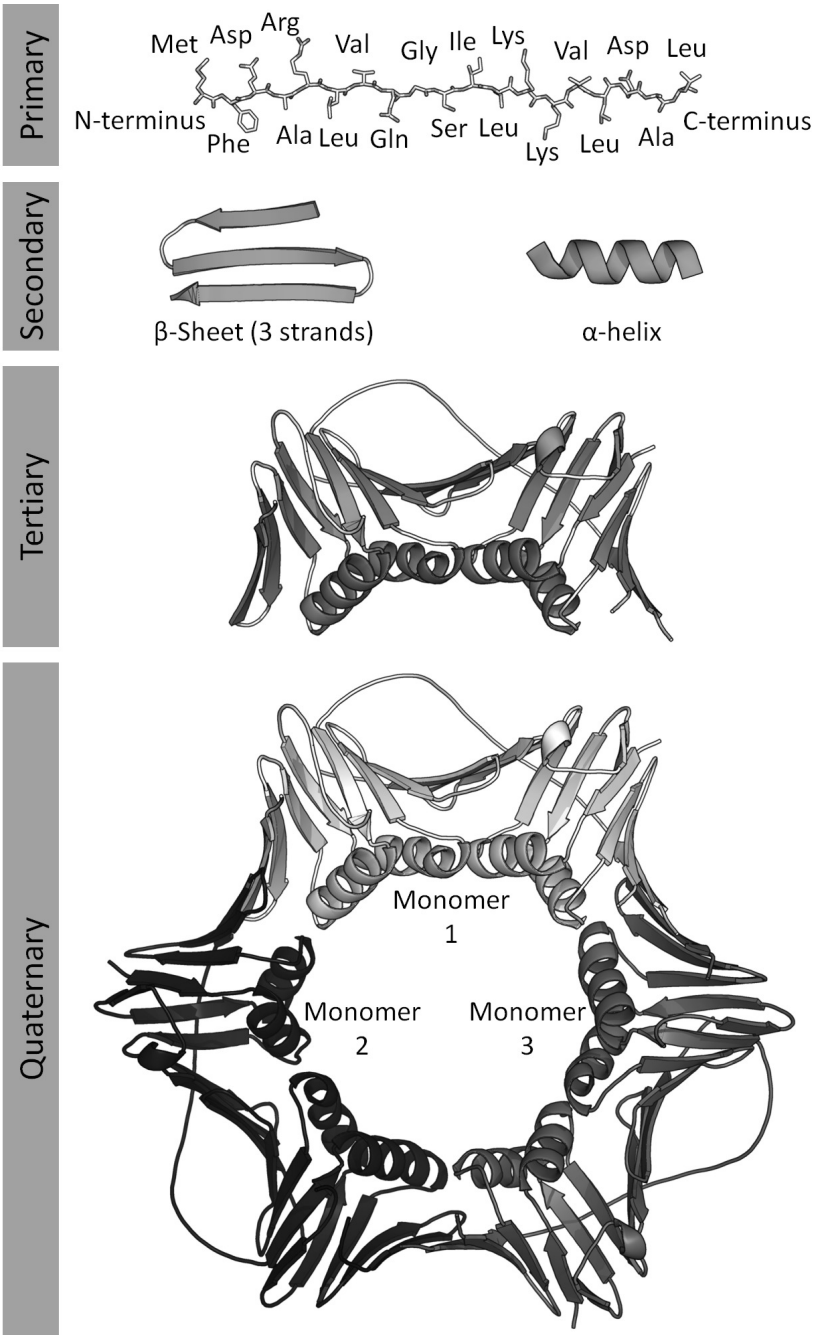


**Figure 2: Confrontation of quaternary structure from monomer subunits with tertiary structure.** [6]

[6] Shafee, T.. *Protein Structure.* Retrieved from https://commons.wikimedia.org/w/index.php?curid=52821068, 2.1.2018. Used Under CC BY 4.0.

## 4.2 Proteins as natural kinds

The information on proteins has had its effect also on the philosophical and metaphysical discussion around them. Moonlighting is a capability of certain proteins to perform secondary functions in addition to their basic functions. Moonlighting does not require changes on the structural form of a protein. This has caused a need to revisit microstructural arguments and has brought new support for other, competitive theories.

While microstructuralism may be able to answer many arguments raised against it, moonlighting forms the key problem for the microstructural theory. According to Tobin, moonlighting does not sit well with the microstructural view. (Tobin, 2010a, p. 42.) If the secondary functions, performed by proteins, are to be regarded as essential for the sound definition of identity, it seems plausible to claim, the microstructural essentialism has difficulties to fully explain macromolecules. This new information seems to imply functional roles have more meaning to protein's identity than previously thought. However, some philosophers do not find functions, such as moonlighting, insuperable problems for microstructuralism. Those who do, often establish some form of pluralism.

Slater argues that adopting a monistic, microstructural view, and to individuate proteins merely by their chemical structure would disregard the importance of functional roles in the classification of proteins, (Slater, 2009, p. 852). To avoid this, he proposes a pluralistic theory. Like Slater, Tobin is skeptical over the possibilities of monism and in favour of pluralistic position. The variety of protein functions seems non-compatible with the microstructural theory according to which it is the microstructure of a subject that determines its nature. Pluralism on the other hand offers a possibility to give the subject as many definitions of kind as needed.

Similarly to Slater, Bartol (2016) sees little hope for monism in the taxonomical practice of proteins, but, unlike Slater and Tobin, considers most forms of pluralism as

problematic. Bartol introduces his own pluralist theory that narrows pluralism to two. To make a distinction between his own pluralism and those of others, Bartol calls the other forms of pluralism *the permissive pluralism* (Bartol, 2016, p. 532). Under permissive pluralism he places those forms of pluralism that claim there are multiple different and equally legitimate ways to categorize an object to kinds. Bartol states that as these forms of pluralism focus on "physical underdetermination between a protein's initial amino acid sequence (called 'primary structure') and its final folded three-dimensional state (called 'conformation')" they end up in conclusion there are possibly as many valid ways to classify proteins as there are structural properties (ibid., p. 532). To avoid this, Bartol establishes a view he calls "restricted pluralism". For Bartol physical underdetermination is not a problem but, as he states, on its own it is not enough to explain the physiological roles of proteins. (Ibid., p. 533.)

Bartol emphasizes neither structural nor functional classification may be privileged over the other without losing important information regarding the identity. Hence, he offers a theory of two kinds as a solution. Compared to more permissive forms of pluralism Bartol says his view is about two very different kinds and interaction between them. For Bartol biological kinds are made by their evolutionary development while chemical kinds are what they are in virtue of their structural properties. According to him, natural kinds are built of two sets of kinds; biological kinds and chemical kinds (Bartol, 2016, p. 548–550.)

Bartol's theory offers a promising but in the sense of Occam's razor more complicated explanation of natural kinds than monism. If we are not willing to accept Bartol's solution, we need to look for alternatives theories. While the monism seems to have severe problems in reaching the sufficient definition in the case of macromolecules, not all are ready to jettison it. According to Goodwin, the arguments against microstructuralism, offered by Slater and Tobin, are inadequate to build a satisfactory theory and therefore a new theory is needed (Goodwin, 2011, p. 533). Goodwin defends

the importance of the primary structure as the basis for the definition of proteins but proposes more versatile version of microstructuralism and therefore is not willing to accept Bartol's view of treating structural and functional properties as different, and equal, kinds (Goodwin, 2011).

On the following chapters some specific abilities of proteins are looked more closely alongside the current theories. I will introduce some persuasive arguments in favour of pluralism and examine some possible ways of how we might revisit the microstructural theory to meet the new challenges. While we might be able to categorize objects and substance in multiple ways and to consider these different ways important for our knowledge, does this mean we should consider the essence of objects pluralistic? Or can the microstructural theory explain the versatile functions of macromolecules?

# 5 Microstructuralism and proteins

It has become evident proteins have functions that seem to fit poorly to microstructural view. Some of their functions are not straightforwardly reducible to the chemical structure or at least it seems the microstructural theory faces some excessive problems while trying to fit these functional capabilities to its theory frame. Functions, such as moonlighting, are troublesome for current theories, but on the other hand they provide a possibility to revise theories altogether. Even more, if our scientific understanding is rooted on taxonomical practices that have trouble in explaining dynamic functions of proteins, clarifying them offers us a possibility to better understand the relationship of functions, structure, and evolutionary development.

Emma Tobin seeks to clarify protein classification by examining their ability to moonlight. Moonlighting proteins have a potential to perform secondary tasks. Whether they do so, depends on different environmental factors. Tobin categorizes moonlighting

in two types: extrinsically structured moonlighting (ESM) and intrinsically unstructured moonlighting (ISM). In the cases where protein extrinsically moonlights, its functional roles are altered by extrinsic contextual factors. Tobin considers these kinds of cases unproblematic for microstructural essentialism, since the function is changed by environmental changes of molecules. However, in cases of ISM structural formability and factors enable the same primary structure to perform different functions. Tobin claims these kinds of situations cause problems for microstructural essentialism. (Tobin 2010a, p. 42.)

Moonlighting is by no means a rare phenomenon, even though it is fairly recently found. Moonlighting is found in many species and there is a wide range of different kinds of functions moonlighting proteins perform (Huberts & van der Klei, 2010, pp. 520–521). Many of the moonlighting proteins have been found from yeast, but it is common also with more complex species (ibid., pp. 520–521). Therefore, it is unlikely that moonlighting can be ignored as an anomaly that is not essential for proteins.

As the moonlighting has been first time excessively studied and reported by Piatigorsky and Wistow as late as in 1980's (Piatigorsky & Wistow, 1989), the studies have caused a need to review some of the earlier established theories regarding the relationship of structure and function in proteins, as well as the relationship of genes and proteins. The diversity of functional capabilities is challenging the notion of a simple causal chain from nucleic acid to amino acid and to a ready protein. Biochemists understand now, that the forming and folding of a protein is much more complex process than previously thought and it involves many different stages from which the protein gains its functional properties. This means that a proper description of a protein requires a more careful examination that chemical structure alone. If a protein and its functions are not dependable only from its genetic structure, the straightforward reduction to a chemical structure might not be able to describe these properties. While microbiologists are currently interested in finding new moonlighting proteins and explaining how proteins

are able to moonlight (Huberts & van der Klei, 2010, p. 523) the philosophical implications of the findings should be also considered. Such implications are for example how moonlighting affects (if it affects at all) our current understanding of classification practices and what we consider as the fundamental essence of proteins.

Those skeptical of microstructuralism have offered several counter arguments against it. While moonlighting offers a fairly recent counter argument, many of the other arguments against the view have been much discussed in philosophical literature. Most of the counter arguments focus on the relationship between chemical structure and the functions. They claim that the thesis reduces the essence of an object to a chemical structure to such extend that the theory is insufficient to explain different essential functions (see Needham, 2011, pp. 4–8). However, because microstructuralism is considered compatible with natural sciences and especially with chemistry, it has still many supporters.

Tobin names three main counter arguments against microstructuralism (Tobin, 2010a). According to her, it depends strongly on the description we give to microstructuralism how well it is able to answer the counter arguments. (Ibid.) In the following chapter I will introduce her definition on microstructuralism as well as considerations on how well microstructuralism is able to answer to the counter arguments raised against it. According to Tobin microstructuralism can respond to most of the challenges. However, moonlighting is problematic for microstructuralism and therefore raises a need for an alternative theory (Tobin, 2010a).

Like Tobin, Havstad examines the microstructural theory and the challenges it faces. Havstad seeks ways to strengthen the theory and while doing so, she argues the chemical kinds are no tidier than biological kinds. It is often thought the chemical kinds are easy to describe while the biological kinds have long been held as difficult case for philosophy. There has been much debate on whether the biological kinds are kinds at all, and if they are, what kind of kinds they are. On contrary to this view, Havstad claims

both kinds are messy in their own way and therefore the clear description of chemical kind is not as easy to make as it is often considered. (Havstad, 2017, pp. 1–2.)

The complexity of biological kinds might have been one of the reasons why scientific practice and microstructuralism have been more prompt to seek definitions form the world of chemistry. However, if, as the functions of macromolecules suggest, the biological traits are important for the description of a macromolecule, the taxonomical order of chemical kinds is gained by leaving out essential information regarding the kinds. If the chemical structure cannot explain essential biological traits, the “tidiness” is actually lack of information. As if a messy room had been cleaned by taking away all the furniture out and by removing the doors: the result is clean, but not perhaps describing the room as it is in normal conditions. Therefore, if we wish to find a definition that is able to reach the various aspects of macromolecules, we need to accept the possibility that things may get messy. That is of course because the tidy order has been illusionary from the beginning. With that in mind, we need to drag all the clutter out of the closets of microstructuralism if we are trying to find an explanation that does not have trouble in cases like proteins.

## 5.1 Microstructural thesis and the counter arguments

Tobin makes distinction between three different kinds of microstructuralism. The first, and the least controversial, thesis makes no metaphysical claims and merely states that members of chemical kind can be classified "based solely on properties of the constituent parts of each member" (Tobin, 2010a, p. 43). The first microstructural thesis goes:

> "(M1) If K is a chemical natural kind and x is any object (sample etc.) then whether x is an instance of K depends purely on the microstructural properties of x." (Tobin, 2010a, p. 43.)

The second thesis is stronger. According to it, chemical kinds themselves have properties and to have these properties is required for the membership of kind (Tobin 2010, 43). However, Tobin notes the second thesis makes no claims about what the properties are and what is their nature (Tobin, 2010a, p. 43). The second microstructural thesis goes:

> "(M2) If K is a chemical kind, then there is a set of microstructural properties S1.....Sn such that possession of these properties is necessary and sufficient for membership of K." (Tobin, 2010a, p. 43.)

Third microstructural thesis is involving a metaphysical claim, according to which all the chemical reactions are caused by the essential properties of kinds and the microstructural properties are the very essence of the K (Tobin, 2010a, p. 44).

> "(M3) If K is a chemical kind, then there is a set of properties S1.....Sn that constitute the essence of K (such that the possession of these properties is necessary) necessary and sufficient for membership of K), and these properties are all microstructural." (Tobin, 2010a, p. 44.)

The third claim includes the view, that also the chemical reactions are determined by the essential properties of the source materials (Tobin, 2010a, p. 44). Tobin names this thesis as *essentialism* in contrast of the weaker theories (Tobin, 2010a, p. 45).

According to Tobin, how well microstructuralism is able to answer to the counter arguments depends on strongly on which of the three formulations of thesis we take to be the microstructuralistic view. Tobin introduces the most often raised challenges. Firstly, isomeric compounds have the same elements in same proportion, but they are arranged differently, and their chemical and physical properties differ from each other. According to Tobin, isomerism does not cause problems to weaker microstructuralism (M1 and M2) however the stronger versions of the thesis need some re-modification (Tobin, 2010a, p. 45).

> "For M1, whether a sample of the hydrocarbon $C_5H_{12}$ is a member of that kind depends purely on its microstructural properties; carbon and hydrogen in the proportion 5:12. For M2, if K is a chemical kind $C_5H_{12}$, then the possession of the microstructural properties of carbon and hydrogen, in the proportion 5:12 will be necessary and sufficient for membership of K." (Tobin, 2010a, p. 45.)

This means the spatial arrangements and other physiological differences are not relevant for the classification in thesis M1 and M2. M1 thesis is interested of the samples properties, which validate the possible classification of the sample in the correct kind. For the M2 thesis it is necessary for the K to have specific elements in certain proportions in order for it to have the membership of K. As all the isomers fulfill these requirements the isomerism does not raise a problem for M1 and M2 (Tobin, 2010a, p. 45). To examine the same example in the context of stronger microstructural thesis, Tobin introduces a fourth thesis:

> "(M4) If K is a chemical kind, then there is a set of microstructural properties S1.....Sn such that possession of these properties is necessary and sufficient for membership of K and those properties concern only the nature, quantity and structural arrangement of the constituent microstructural parts." (Tobin, 2010, p. 45.)

Here the structural arrangement is raised as a relevant property of classification. According to Tobin, M4, as well as M3, have much more difficulties to answer to the challenge of isomers. M3 claims certain properties are essential, necessary properties of K. In addition to this, they are necessary for the membership of K. For microstructural essentialism the set of necessary properties is microstructural. Tobin notes, that a supporter of M3 or M4 thesis might offer a view that spatial arrangement is constituent part of microstructure or continuation for it. (Tobin, 2010, p. 45.)

According to Tobin, microstructuralism does not need to be concerned about the molecular shape: if the shape is viewed as an extrinsic property for which "the atomic microstructure provides a sufficient restraint", M3 and M4 are able to answer to the

challenges caused by isomerism. Microstructuralism can also answer to the challenges regarding the environmental conditions and how they affect the molecular shape. According to Tobin the claim "refers to the chemical kind itself rather than instances of the chemical kind in environmental conditions". Thus, even the changes caused by the change of phase do not cause an insurmountable obstacle for microstructuralism. (Tobin, 2010a, p. 46.)

Another problem microstructuralism faces is whether it may be extended to the compounds. The core of the argument is, that macroscopic bodies enable the identification and the identification cannot be done without taking into account macrolevel properties. For example, in the case of water many of its characteristic properties are of macrolevel.

Needham argues that these macroscopic properties of water are not only possible but furthermore can give adequate description of water without a microscopic description. The root of Needham's thesis is, that a possibility of macroscopic description counters the claim that microscopic description determines the identity of substance. According to Needham microstructuralism is insufficient to capture the essence of a chemical kind. (Needham, 2011.) Because of the unique thermodynamic properties of water, only macroscopic samples can be identified as water (Tobin, 2010a, p. 46).

To avoid the problem caused by the macroscopic properties, Tobin introduces Robin Findlay Hendry's (2006) definition for water. According to Hendry we may agree that merely a chemical form $H_2O$ is not able to capture all the macroscopic properties of water. This is because the sameness of elemental composition is necessary (yet insufficient) condition for the identification of a compound. (Tobin, 2010, p. 47; Hendry, 2006.)

To clarify his thesis, Hendry makes a distinction between ingredients and components. Ingredients are used in the process of making the compound while components survive

the process and persist in the product compound (Tobin, 2010a, p. 47; Hendry, 2006, p. 873.) As Hendry summarizes: "The elemental composition condition of substance identity requires that elements are components of substances, not mere ingredients" (Hendry, 2006, p. 873). On basis of these new definitions Tobin formulates the fifth microstructural thesis:

> "(M5) If K is a chemical kind, then there is a set of microstructural properties S1.....Sn such that possession of these properties is necessary and sufficient for membership of K and those properties concern only the nature and quantity of the "components of the kind." (Tobin 2010a, p. 47.)

According to Tobin, microstructuralism in the form of M5 is able to answer to the challenges caused by structural properties and re-combination (Tobin, 2010a, p. 47).

The third challenge for microstructuralism is whether it is able to explain macromolecules (e.g. polymers). As discussed earlier, in addition to structural properties of individual molecules, also physical arrangement is significant for the macromolecules and their functions. Furthermore, as Tobin points out, the molecular environment influences polymers and therefore is more fundamental part of the polymer structure than in the case of smaller compositions. (Tobin, 2010a, p. 47.)

Polymers are molecules consisting of several small molecules, monomers. Heteropolymers, also called as copolymers, are polymers consisting of several different kinds of monomers. Homopolymers on the other hand, are consisting of single kind of monomers. Especially copolymers are problematic for microstructural theory (Tobin, 2010a, p. 47). In copolymers monomer chains can form connections, which affect the properties of polymer and the size of polymer affects its properties, thus making it difficult to reduce its properties neatly to the fundamental chemical structure or to its monomers (ibid., p. 47).

> "The shape of a polymer affects the properties that we use to classify polymers into higher-level kinds. For example, elastomers refer to polymers that are above their glass transition temperature. These macrostructural properties might be considered crucial to classifying higher-level macromolecules into natural kinds." (Tobin, 2010a, p. 48.)

Tobin claims even the weaker versions of microstructuralism struggle to answer to the problem. The examples introduced earlier indicate the macroscopic properties are important part of the classification of x. For example, in the case of M1 also macroscopic properties define whether x is an instance of K. Therefore, is seems problematic to claim that only the microstructural properties are able define the membership of x, like M1 theory claims. Additionally, the stronger versions of microstructuralism have difficulties when describing polymers. M3 theory argues there is a set of properties constituting the essence of K and these properties are necessary and sufficient for the membership of K. According to M3 theory these properties are microstructural. However, according to counter-argument, also macroscopic properties are an essential part of K. Similarly, M4 has problems with this counter argument. (Tobin, 2010, pp. 48–49.)

Though the challenge seems real, Tobin, in contrast to Needham (2011), considers microstructuralism able to answer to the counter-arguments. This is because the higher-level properties can be considered as a direct result of the microstructure:

> "The geometry of cross-linked, branched and network polymers is a direct consequence of the monomers involved and their covalent bonds. For example, the glass transition temperature is a direct result of the presence of side chains off the main chain, which increase the class transition temperature of the polymer by restricting bond rotation. Therefore, the microstructuralist can respond that the molecular classification of the individual monomers and the bonds they enter into can at least in principle determine subsequent macrostucture" (Tobin, 2010a, p. 49.)

Therefore, while Bartol (2016) considers these molecular properties too problematic for microstructuralism and suggests there should be an alternative way of classifying and

identifying macromolecules as kinds, Tobin considers microstructuralism able to answer this. Moreover, counter thesis does not cause problem for M5. (Tobin, 2010a, p. 49.)

## 5.2 Moonlighting

Biopolymers, such as proteins, cause new problems for microstructuralism. As a part of an organism, protein's structure is driven also by its surroundings and in interaction with it. The tertiary structure alters depending on protein's environmental factors to extent where the different final protein is produced.

While Tobin considers microstructuralism well equipped to answer to most of the arguments against it, she suggests moonlighting proteins are too problematic for the theory (Tobin, 2009). When proteins moonlight, they fulfill several additional functions (Jeffery, 2004, 2009; Tobin, 2010a, p. 50). For example, structurally similar crystalline proteins can fulfill distinct functions. Tobin stresses that crystallins can be seen as part of several macromolecular kinds. They have functions of enzymes, structural proteins as well as serve as globular proteins (Tobin, 2010a, p. 51). While functional changes caused by changes in molecular environment can be considered un-problematic for microstructuralism, not all cases fall under this category.

However, *intrinsically structurally disordered* moonlighting proteins are a bigger challenge for microstructural theory. These proteins have properties that enable them to behave more flexible than most of the proteins. None of their functions may be clearly claimed as original. (Tobin, 2010a, p. 51.)

According to Tobin all forms of microstructuralism face difficulties with moonlighting proteins. Therefore, none of the current theories of microstructuralism can answer to the challenges by moonlighting proteins in satisfactory way (Tobin, 2010a, p. 54). However, Goodwin claims Tobin has misunderstood the hierarchy between the

structural and chemical properties (Goodwin, 2011, p. 534). According to him, we need to clarify our understanding on the role of structures in order to understand how macromolecules, such as proteins, are classified.

While both Tobin and Havstad introduce and examine various problems in microstructuralism, Havstad is not ready to jettison microstructuralism right away. Instead, she considers some of the ways it could be remolded to meet the new problems. (Havstad, 2017, p. 3.) Havstad approaches proteins by examining the similarities and differences of biological and chemical kinds. She examines closely especially the arguments by Hendry and asserts that his account of chemical kinds and microstructuralism is not as inclusive as it is often considered to be. According to Havstad it is also far from clear that the chemical kinds are same as the microstructural kinds. (ibid., p. 13.)

To support this view Havstad goes through different problems associated with mixtures and how able microstructuralism is to describe them. Mixtures may be distinguished to single-state mixtures, multi-state mixtures and colloidal mixtures. Mixtures such as concrete are problematic for traditional microstructuralism. (Havstad, 2017, p. 13.) Havstad expresses the problem in following way:

> "If sameness of elemental composition is a condition for sameness of chemical substance, then the term 'concrete' turns out not to refer to one chemical substance after all—it refers to many different chemical substances instead. There would be a distinct chemical substance for each sample of so-called concrete with a unique elemental composition—potentially, one for every extant sample." (Havstad, 2017, p. 14.)

Obviously, this sort of variety is not desirable for supporters of microstructuralism, especially if they are after a theory that is in balance with scientific practice. With that in mind, we may question whether the *sameness of elemental composition condition* is a blanket condition or is there other ways to give a definition to sameness of chemical

substance (Havstad 2017, 14). To avoid the contradiction emerging from this, microstructuralist could refine the case and specify that the sameness of elemental structure is required *only for chemical kinds*: "On this reading, the sameness of elemental composition condition would only be a requirement for sameness of chemical kind, not for sameness of chemical substance." (ibid., p. 14.) However, since for Hendry the chemical kinds *are* chemical substances this does not save his theory from contradiction (ibid., p. 14).

According to Havstad, compounds like proteins have similar problems in fitting in the requirements of the microstructural theory. There are many different proteins, which all are considered as members of the same chemical kinds (Havstad, 2017, p. 15.) Havstad stresses that even when viewed on species-specific lever, there are differences in the primary structure. Alleloforms are variants of certain protein. Despite of the differences in their primary structure their higher order structure and functions do not differ from each other. (Havstad, 2017, p. 16; see also Slater, 2009.)

Because of alleloforms and isoforms[7] the sameness of elemental structure can be seen as an unfit way to categorize proteins (Havstad, 2017, p. 16). How can microstructuralism explain the different isoforms? If the theory allows (specific) different structural differences, can it still ground the kindhood in microstructure? Does admitting so imply microstructuralism accepts there is something else than its (unchanging) structure that is making a protein what it is? If a protein can be made of

[7] Structurally different proteins, which also have some functional and higher order differences.

different structures, a protein, per se, does not seem to be merely the same as its structure[8].

# 6 Functions and the structure

According to Goodwin, we can avoid many of the problems faced by monism, without accepting pluralism, by allowing alternative levels for classifying things. When monism, or microstructuralism, is not limited to have its definitions only from the microstructure, explaining functional characteristics becomes easier. Goodwin suggests we should not adopt pluralism, as this would mean accepting several equal ways to define substances. However, he acknowledges monism in its traditional sense has difficulties in answering the questions raised by functional characteristics, such as moonlighting. Goodwin offers a new way to define monism. He suggests we should allow additional levels for the definition of kind. This enables the definition not to be reduced to the microstructure, from which it however gets its grounding essence. (Goodwin, 2011.) This kind of theory gives us more adaptive theory that is also more capable in answering the counter arguments against microstructuralism. However, it is more complex than simple microstructuralism or pluralism.

Goodwin points out that in scientific practice biologists use many additional ways to define proteins depending on the research needs, but this does not imply the researchers would consider all these definitions equal. Instead, the functional definitions can be viewed as supporting, additional ways to describe the essence of

[8] As structure is something it *has*.

proteins from a different perspective. These kinds of added levels make the definition richer and more able to reach the diversity of properties and functions proteins hold. (Goodwin, 2011, p. 536.) It may be claimed that one of the reasons why metaphysics and philosophy of natural kinds have had problems to describe macromolecules in satisfactory manner is that philosophers have sought a clean, tidy definition for a complex composition that holds many functional roles and has several potential structural forms.

While Needham considers variety of functions as a sign for pluralism and against monism (see Needham, 2011), monism might well be able to survive from moonlighting. Indeed, turning to pluralism seems to be related to the similar seek of tidy definition as why many philosophers find the traditional monism appealing. While Slater calls microstructuralism as a search of clean definition in "a messy world" (Slater, 2009, p. 851) we may well say accepting pluralism can be seen the same way. However, a clean definition might not be the best way to approach biological, dynamic structures developed to answer variety of demands set by their host organisms. Both, strong monism and pluralism, avoid a context-aware evaluation, which might well be the only way to understand the dynamic nature of biological components and organisms. Therefore, too narrow definitions might not be the best way to approach biological, dynamic structures developed to answer variety of demands set by home organism.

For example, property of water is easier to define if we are able to shift our perspective and give water several descriptions that all define it. Even while doing so, we might ground the definition to the microstructural properties by considering them as most essential for the identity. Goodwin seems to follow the same track of thoughts by claiming that while we may consider molecular structure fundamental for the definition, other explanatory levels need not be reductive to that (Goodwin, 2011, p. 540). Many of these levels can be understood as "potentialities of a molecule" (ibid., 540). These

potentialities do not necessarily actualize, but, never the less, they are part of its essential properties.

If we consider Tobin's arguments again, it is obvious the strongest arguments against microstructuralism are functions such as moonlighting. At least Tobin (2009) and Slater (2017) are pessimistic about microstructuralism's capability to meet the challenges. Similarly, Needham (2011) is ready to jettison microstructuralistic theory. Goodwin claims their arguments are grounded on stereotypical notions of microstructuralism and misinterpretation of the theory (Goodwin, 2011, p. 535). According to him, various classificatory practices are not in contrast and may be included as a part of monistic understanding of proteins. Furthermore, Goodwin continues that even molecular chemists use several ways of classifying the macromolecules and do not base their classifications merely on the molecular structure. (ibid., p. 538). However, this is not to be taken as a shift towards pluralism. According to Goodwin, primary structure does not need to explain all the abilities of proteins in order to be the fundamental explanatory level.

## 6.1 Bartol and Goodwin: new ways to classify macromolecules

Should we hold on to microstructuralism even if it has such difficulties to describe macromolecules? Main reason to support this view is that microstructuralism appears to be in ideal balance with nature sciences and scientist of physics and chemistry share the microstructural view. It also offers an adequate explanation and is coherent and, at least seemingly, simple. Microstructuralism offers a solid ground on which to build a coherent theory; pluralism on the other hand seems much harder to put down in a simple thesis. However, as we have taken a closer look of the different counter theses it becomes clear microstructural thesis is not as tidy as it seems. If we need to add more

levels or to divide the microstructuralism in different additional explanatory levels, it loses some of its easiness. Bartol claims this is a strong argument for a search of additional ways to classify things (2016).

Even though Bartol admits monism appealing, he calls the tidy ontological reduction to biological or chemical kinds impossible and offers this as an argument for pluralism (Bartol 2016, p. 532). However, monism being messy does not yet imply that pluralism would do any better. For Bartol, also pluralism in its permissive form is unsatisfactory (ibid., p. 532). According to him, philosophers are drawn towards accepting pluralism because of the physical underdetermination of protein's primary structure and its conformation state (ibid., p. 532). Bartol claims this is the central reason also for Slater and Tobin to adapt pluralistic theory (ibid., p. 532).

According to pluralists like Slater and Tobin, the different structural arrangements are physico-chemical kinds in their own right. To this end, Bartol does not consider it problematic for two chemical kinds to have the same microstructural structure and yet differ on a macrostructural scale. According to him we may take this potential of molecules as something they have due to the structural characteristics. Different final arrangements are therefore results of the microstructure and are not problematic for the microstructural theory. (Bartol, 2016, pp. 540–542.)

However, Bartol considers microstructuralism incapable of answering many questions related to biochemical kinds and functions (Bartol, 2016, p. 543) he suggests we should adopt a dualism of kinds in which the chemical and biological properties are to be viewed as separate kinds. In this reading, proteins are both biological and chemical kinds without either one to be reduced to the other (Bartol, 2016, p. 543).

The etiological view claims the evolutionary trait is what makes the species, or macromolecules, what they are. When viewed this way, current microstructural properties are part of the history but not what makes things what they are (Bartol, 2016,

p. 546). What makes the etiological theory appealing is that structural changes are not as problematic for the etiological theory as they are for microstructuralism. Changes on structure and function are often considered problematic in discussion of biological kinds. Bartol explains they do not cause problem if we are able to shift our focus from microstructural theory towards a theory that takes into account the both; structural and functional aspect. Therefore, Bartol claims neither structural nor functional changes determine whether proteins are similar or not, as it is the historical traits that determines it (Bartol 2016, p. 546–547).

Offering a view according to which there are two categories of kinds Bartol aims to avoid the pluralism of taxonomical practice. His theory has two categories of kinds, but they do not describe the same object and therefore the pluralism of taxonomical practice is avoided. Indeed, Bartol claims that functional and structural characteristics of proteins should be understood as of two different units. Bartol is aware his views do not fit well with actual scientific practice. However, as he claims, this should not be viewed as a disadvantage since our metaphysical theories should not be axiomatically subordinated to practices of science. (Bartol, 2016, p. 548.)

For Bartol, there are no biochemical kinds as a separate class of kinds. Biochemicals are what they are based on their taxonomical status as chemical kinds and biological kinds (Bartol, 2016, p. 549). Bartol also claims the main reason why biochemists have concentrated on structural properties of proteins is that the evolutionary background is still insufficiently known. Therefore, it has been more meaningful for biochemists to concentrate on structural properties. While Goodwin considers biochemists primarily interested of structural properties of proteins (Goodwin, 2011, p. 534) Bartol claims this should be understood as a pragmatic trait of scientific practice and not as a metaphysical argument for reductionism (Bartol, 2016, p. 549). It is because of an epistemic barrier that we are unable to unravel the evolutionary history and to fully understand the biological classification (ibid., p. 549). However, we may propose this should not prevent

philosophical contemplation on the matter even if scientific practice is restricted by it. It is well possible to explore the different classifications and arguments supporting them, even if the actual historical knowledge is incomplete.

> "While metaphysicians want their results to hold over all possible worlds, across all possible conditions, real-life scientists tend to work in just one actual world, and even then in a fairly circumscribed range of actual conditions. It is perfectly acceptable if they fine-tune their taxonomy to this world and those conditions. Yet when we set practice to one side we can see that, when it comes to biochemicals, nature has two sets of joints." (Bartol, 2016, p. 550.)

Therefore, according to Bartol, it is not self-evident that the taxonomical practices of scientist should be viewed as determining ground rules for metaphysical enquiry (Bartol, 2016, p. 550). Of course, this is not to say they are contradictory. Even if purposes and motives for scientific and philosophical practice are different from each other and engaging in different methods, it does not follow from this that they do not investigate the same objects or phenomena. However, the questions and the perspective are different.

## 6.2 Perhaps pluralism then, after all?

Mitchell and Gronenborn reflect the thoughts of John Kendrew, who examines various problems in protein folding. Mitchell and Gronenborn do not find it surprising Kendrew found it difficult to come up with satisfactory explanation. According to them, the behavior and structure of proteins is so complex, it requires a theory that is able to explain all the various functions and structural changes among proteins. Mitchell and Gronenborn claim this is a call for pluralism. (Kendrew, 1963; Mitchell & Gronenborn, 2017, p. 705)

According to Mitchell and Gronenborn, if proteins were performing their functions without interaction with their surroundings, microstructural, monistic explanation might be adequate (Mitchell & Gronenborn, 2017, p. 710). However as the functions are dependable also from other external functions, Mitchell and Gronenborn consider microstructuralism lacking explanatory power (Mitchell & Gronenborn, 2017, p. 710). Similarly to Bartol (2016), Mitchell and Gronenborn note that there are no necessary relations between scientific practice and philosophical research. Since for scientific practice only those aspects are meaningful which scientist meet in their studies, taxonomical practices of scientists may not be used straightforwardly as guidelines for philosophical inquiry (Mitchell & Gronenborn, 2017, p. 706).

Mitchell and Gronenborn point out that while it has been commonly thought that the microstructure of a protein is responsible of determining the functional abilities, also the external factors bear important role. The full understanding of proteins is therefore possible only by taking into account factors such as temperature and interaction with surroundings. Even though there are some proteins that able to perform on their own, most are dependable of other proteins or surrounding tissues. (Mitchell & Gronenborn, 2017, pp. 709–710)

Slater points out that for the biochemical taxonomy the biochemical function is often more important than the chemical structure of a protein. Though the folding of a protein might seem like compatible with microstructural monism, Slater claims it is the very opposite. The folding is not a simple reductive chain from the microstructure to the higher lever functions. Instead, many properties of protein emerge from the folding, not from its amino acid sequence.

Slater reminds that the amino acid sequence alone does not tell us much about proteins final role, since there are multiple ways by which the same amino acids structures can fold. Since the folding plays such a central role in possible functions of a protein,

reducing the nature of a protein to its amino acid sequence is problematic. (Slater, 2009, p. 852.)

Mitchell and Gronenborn also claim we should follow the models used by science when we seek for satisfactory explanation. As there are several scientific models, pluralism is the only option. (Mitchell & Gronenborn, 2017, p. 711) However, I think it is important to bear in mind that taxonomic choices of scientist are often pragmatic decisions, and do not imply that even the scientist herself is engaged in thinking all the different models are equal. With that in mind, another important question is what the relation between the scientific explanation and a philosophical one is. Are they necessarily the same, uncontradictory and moreover, are they aiming for the same goal?

Should we accept pluralism in the context of philosophy merely on the grounds of that science uses multiple models? The pragmatic practices do not necessary express ontological claims even if we may consider them to reflect such. As Mitchell and Gronenborn themselves pointed out for pragmatic practices “To be successful, they need to capture (by similarity, isomorphism, structural, or causal mirroring, and so on) features that are relevant to the processes and events we want to understand” (Mitchell & Gronenborn, 2017, p. 706). Furthermore, even if “model plurality and partiality are necessary for scientific understanding.“ (Mitchell & Gronenborn, 2017, p. 705), it may not be the same for philosophical explanation. It may be, but it does not follow straight from the claim.

Basic argument of Mitchell and Gornenborn is following:

P1: If the protein structure and functions are solely determined by the amino acid sequence, the monistic theory can explain proteins.

P2: The Protein structure and functions are not solely determined by the amino acid sequence. Instead, other molecules of surrounding cell influence proteins.

C: Therefore, the theory explaining proteins has to be pluralist.

Slater argues that when molecular biologists examine the protein structures, they do not refer to the "protein's essence" (Slater, 2009, p. 854) since the techniques used are only able to capture the structure in unnatural settings. If we wish to give proteins a definition that is able to capture them as they are, in natural environment, we cannot examine them merely by methods that hinder some of the essential properties of a protein. This means that a definition of a protein which has been artificially prevented from moving and interacting with its surroundings, does not give us a fully explanation of proteins essence. Even if such findings are useful they are, at best, incomplete.

Similarly, Mitchell and Gronenborn point out that while three-dimensional structure of proteins may be examined only in vitro, the functions of proteins are closely connected to their biological surroundings. This means it is difficult, if not impossible, to define which of the different in vitro descriptions we should take as primary explanation. (Mitchell & Gronenborn, 2017, p. 717.)

As in vivo research on microstructure is not yet technically possible to do, there remains a gap between structural knowledge gained from laboratory studies and research on functions. If we have access on structural information and functional information, but no way to combine them, it is hard to see how a coherent theory of proteins may be built. Also, even though these descriptions of structure might be useful in research, and scientists use them when defining proteins, the description of a protein is about it in vitro. This should be remembered when searching any essential description for proteins.

Theories by Goodwin and Bartol intend to seek a middle ground by not accepting pluralism and by admitting the difficulties of the microstructural theory in its traditional form. Of course, finding a theory that is able to explain the wide and diverse functional and structural properties of molecules is not an easy task. It seems, especially in the case of proteins, that examination from multiple angles is needed. Of course, this pulls

towards pluralism. Yet it does not need to follow from this that pluralism should be accepted. We may well consider proteins to be what they are because of their microstructure even if we examine their appearance in various ways (cf., Goodwin, 2011). But if we claim that *a*) proteins are substances, which require multiple ways to classify them, and b) there is no singular, primary way of classification, then monistic theory is not an option for us. Goodwin realizes this and offers his theory as a solution to the problem (Goodwin, 2011).

Bartol's theory of two kinds also aims to solve the same problem but with different means. He narrows the pluralism down to two and introduces these as equal kinds. Accepting Bartol's dualism of kinds means that we have to give up the macromolecular kinds; for Bartol, there are only biological and chemical kinds but no macromolecular kinds. Instead, macromolecules always belong to two different kinds. (Bartol, 2016, pp. 548–549.)

Why then should we see so much trouble in avoiding pluralism? I argue that while pluralism might seem appealing and easy solution, it offers only a partial solution; pluralism seems to fit poorly with classification practices of scientific research and it is intuitively dissatisfactory that multiple different ways of classifying were equal. Even if we don't think the philosophical definitions should always follow the scientific ones, it is important that the scientific definitions should not be overlooked or, even worse, be in contradiction with the philosophical ones. Furthermore, it seems some definitions are more essential and are telling more about the things they define than others. It is notable that in the case of pluralism it shouldn't be so; pluralism considers all different classificatory practices equal and therefore there should not be any primary way to classify things. It is here where Goodwin's theory differs that of pluralism; Goodwin calls for primary classification but claims also that it alone is not sufficient (Goodwin, 2011). Moreover, the additional classifications are needed, because without them we are not able to answer to those counter arguments pluralists have expressed towards monism.

Therefore, Goodwin's theory does not appear to be merely ad hoc correction of previous theory. Instead it offers a different perspective to understand the relationship between biological and chemical world as well as functions emerging from them[9].

## 6.3 Crosscutting categories

Tobin (2010b) considers hierarchy to be one of the key problems for understanding of natural kinds classificatory practice. In her article "Crosscutting Natural Kinds and the Hierarchy Thesis" she asserts the idea that categories should not be crosscutting is itself outdated. Crosscutting categories are viewed as problematic and, because biological categories often are indefinite, they have considered unsuitable as natural kinds (Tobin, 2010b, p. 179). The hierarchy thesis claims there should not be any overlapping of categories. Therefore, for example the category of *quadrupeds* (four-legged animals) is problematic for hierarchy thesis. Tobin gives a following example: dogs can be classified with humans as mammals and with crocodiles as quadrupeds, yet humans cannot be classified with crocodiles or dogs as quadrupeds. Thus, the classifications are crosscutting (ibid., p. 179.)

According to Tobin there is crosscutting also among chemical classifications. For this reason Tobin argues the hierarchy thesis should be rejected. (Tobin, 2010b, p. 189.) Similarly, Ian Hacking considers natural kind categories problematic (Hacking, 2007). He gives a similar example with chemical substances; rubidium-47 may be categorized under boson and rubidium, yet rubidium or boson cannot be classified hierarchically under each other. Hence, there is overlapping of categories and creating a tidy ontological tree with rubidium-47, boson and rubidium is impossible. (Hacking, 2007, p.

[9] Whether we are committed to a view that functions emerge from biological, evolutional development or chemical, structural properties pays no difference here.

214.) It may, however, be claimed that since the taxonomical distinction between boson and fermion is more fundamental, the ontological tree may be built based on this.

## 6.4 Hierarchy thesis as a background structure of current theories

Since all the theories seem to have severe problems to grasp molecules, proteins and to give an explanation to what is a natural kind, should we then just, for the sake of clarity, give up the notion? Perhaps the problem is that we are trying to find a description that is not there. To look this another way, we may agree there are proteins and they have certain properties and functions, but perhaps there are no natural kinds, and trying to find a description of a protein natural kind is difficult because of that.

Tobin examines the underlying problems that are rooted in the structural understanding of current taxonomical practices and derives from this that the hierarchy thesis is problematic. Should we take this as evidence that we would be better off without natural kinds? Tobin thinks not. She argues that giving up hierarchical thesis is not slippery slope towards denying natural kinds in whole. She believes hierarchical thesis to be one of the central reasons why understanding diverse kinds (such as macromolecules) has been difficult but concludes natural kinds themselves need not be jettisoned. (Tobin, 2010b.)

Hacking seems to have been noticed the same difficulty in taxonomical practice as Tobin (Hacking, 2007). He too suggests that the whole idea of natural kinds is based on idealistic assumption of neat, clean categories that in reality do not exist at all (Hacking, 2007, p. 209).

Hacking emphasizes the idea that there are sets called “natural kinds” has its origins in problems that scholastics faced when researching natural groups. When Linnaean taxonomy was put to use, hierarchical structure of beings was standardized. It follows

from the central idea and structure of the hierarchy that, for example, species cannot be genera and vice versa. While the Linnaean taxonomy has enabled biologists to categorize organisms and their evolutionary background it has given rise to problems. (Hacking, 2007, p. 210.)

As our scientific knowledge has increased, the conflicting structures between the contemporary knowledge and traditional classification practices may have become visible. As the traditional classifications have been created before access to the knowledge we have now, we need to review also the basic assumptions the theories are built on.

Like Tobin argued, the hierarchical structure has trouble in understanding the knowledge of latest scientific researches (Tobin, 2010b). According to Hacking, with the new classificatory practice emerged the question whether the concept of class represents the resemblance between individuals and if so, what kind of resemblance should be taken into account (Hacking, 2007, p. 210). It is clear, that depending on what we consider as essential similarity for classification, the categories can be very different kind. For example, if we consider “walking with four legs” fundamental similarity we end up with very different sort of category than if we consider “nursing with milk” fundamental similarity.

Understanding the hierarchy thesis might be the key for understanding why there has been so many obstacles in understanding the status of macromolecules. It has become evident that macromolecules are a diverse group that derives its nature from several distinct properties. Hierarchical thesis does not allow such diversity and therefore theories built on it bear similar problems as the basic theory. Tobin’s central claim seems to be this: as hierarchical systems such as periodic table of elements are not in fact reflecting the natural order, the microstructural thesis cannot be effectively defended with arguments that are based on such assumptions. In other words, preferring microstructuralism because it is in better harmony with taxonomy of chemical

substances will not do if we are after a definition that actually explains what subjects, such as proteins, are. On the other hand, microstructuralism that is not strictly kept in harmony with the hierarchical thesis, and which does not seek its validation from that, can survive from the counter argument.

According to Tobin the hierarchy thesis claims there are two distinct kinds, silver and gold, but no overlapping between them. They belong strictly to different kinds. For two subjects to be kinds, they cannot be categorized into each other unless there is a hierarchy between them. (Tobin, 2010b, pp. 180–183.)

Because of this, proteins are problematic for hierarchy thesis. It was long believed all enzymes where proteins but when it was discovered in 1980's that also RNA has the ability to make the necessary structural changes and to catalyze reactions, it became evident enzymes where more various taxonomical group than previously thought. RNAs, such as the hairpin ribozyme, can be classified as enzymes, as well as protein renin. Renin belongs to albumins that are water-soluble proteins. However, not all albumins are enzymes. Therefore, Tobin points out, even though renin and the hairpin ribozyme are both enzymes and renin and albumin are both proteins, the hairpin ribozyme and albumin cannot be classified together to ether one, proteins or enzymes. (Tobin, 2010b, p. 183.)

Tobin admits the hierarchy thesis may be defended by arguing RNA and DNA are both nucleic acids and this would be "the underlying kind of which both enzymes and proteins are composed" (Tobin, 2010b, p. 184) However, this would overlook many distinct properties of RNA and DNA (Tobin, 2010b, p. 184).

Despite of this, Tobin does not suggest discarding natural kinds altogether, or ruling out all those that are overlapping each other. Instead, Tobin suggests we should allow natural kind classifications that do not form clean, "simple nested hierarchies". Tobin argues the difficulties faced by the hierarchy thesis while trying to categorize RNA and

DNA based enzymes as same kind indicates there are fundamental differences that should be taken into account. Even more, to overlook the differences for the sake of hierarchy thesis would be to disregard many interesting and important qualities of different proteins and enzymes. (Tobin, 2010b, p. 189.)

In conclusion, crosscutting categories are a challenge for the traditional view of natural kinds but that should not keep us from considering them as a part of what natural kinds may be. Like many other aspects of research on macromolecules, this too implies there are previously ignored parts of classification practice that need to be taken into account. Understanding the problems with crosscutting categories might help us to understand the difficulties on finding a definition for diverse structures such as proteins. Therefore, instead of engaging in hierarchical position, a categorical practice built in a form of net, might be more efficient to explain the grey areas of taxonomy. This kind of remodeling of the root assumptions is not exceptional in nature sciences. The phylogenetic tree has gone through the same kind of shift as it has been shaped in less hierarchical form after the increase of genetic and evolutionary knowledge at the beginning of 21th century (see Hug et al., 2016).

# 7 Etiological approach on functionalism in Biology

Since reducing functions in terms of microstructure appears to be the biggest obstacle to the microstructural theory, in the following chapter I will take a closer look of the different theories on the biological functions and how they explain functions. Functions evolve because they have previously been an asset for the organism and its survival. The etiological theory considers the history of a species or organism crucial for defining it (Godfrey-Smith, 1994, p. 1). The biological functions explain why a certain trait has been successful in the natural selection (ibid., p. 1).

## 7.1 Etiological theory

If we consider the evolutionary background essential in explaining the nature of things, microstructuralism appears insufficient for explaining functions, that, by their definition, are historical. If functions are important for molecules existence by being responsible for why the host organism has survived, reducing functions to microstructure seems problematic. For etiological theory functions are not only explaining the existence of a macromolecule, but also what a molecule is.

Let us consider for example an apple. An apple is the reproductive mechanism of an apple tree. The trait has survived because the function of producing apples has been a successful method of reproducing for apple trees. However, does this mean we cannot give a proper description of an apple without knowing this? The full understanding of “applehood” might be difficult without knowledge of apple’s function, but nevertheless it seems we can give a description of it. However, according to etiological theory, the explanation that is given without taking into account the history is not a proper one.

Sandra Mitchell supports etiological approach and traces the nature of functions to the development history of species and organs. In the etiological theory a function is “a consequence of some component of a system”(Mitchell, 1995, p. 39). It is also important that not any consequence is fit for function. For consequence to be a function it must have “played an essential role in the causal history” and therefore to have been a key reason for a trait’s or component’s survival (ibid., p. 39). This means that for example moonlighting can be considered as a function of a protein if it has been and crucial part of proteins evolutionary history. For Mitchell and for the etiological theory “to explain why something occurs is to describe the causal history which led to the event – i.e. to give its etiology” (Ibid., p. 41).

According to this we may explain moonlighting, not by structural properties of a protein but by the development history of moonlighting proteins. For the etiological theory to know the evolutionary background and the reasons why moonlighting has been an asset for proteins is to know why the function exists and what it essentially is.

In other words, when considering protein’s functions and their status as natural kinds, etiological theory seeks the explanation from a different direction than microstructural theory. Since for etiological theory the history of the trait is essential, the knowledge of structural properties is not necessary. For example, when explaining functional abilities of crystalline protein, etiological theory explains the function by specifying how and why the moonlighting ability has evolved and persisted. This, of course, means that if we are to accept etiological theory it becomes difficult to hold on the microstructural account.

I understand that this is why Bartol has ended up dividing the definition of macromolecules in two kinds and denies macromolecular kinds as a separate class of kinds. Bartol’s theory can survive from accepting etiological view, as the etiological explanation is compatible with his biological kinds. (2016, pp. 545–547.)

There is more tension between Goodwin's theory and etiological view. Goodwin allows additional explanatory levels, but in his thesis there is evident hierarchy between different levels in a sense that the chemical structure is always fundamental (Goodwin, 2011). Etiological theory, on the other hand, considers the historical background primary for defining the functions. Therefore, for Goodwin etiological theory can, at its best, give only an additional explanation for functions while the fundamental explanation remains microstructural.

To elaborate etiological theory, Mitchell introduces few different interpretations of etiological view. Mitchell stresses that malfunctioning organisms cause problems for etiological interpretation. "If one insists that each individual X must result in Z if Z is a function of X" malfunctioning heart does not have the function of pumping blood whereas a healthy heart does (Mitchell, 1995, p. 44; Millikan, 1989; Prior, 1985). On the other hand, this differs from such cases where X has the capability to result Z in the right circumstances (Mitchell, 1995, p. 44).

Certain traits have survived in the evolutionary history of the subject because the trait has in some way been an asset (Mitchell, 1995, p. 42). This has caused the subject to develop in a certain way. Mitchell argues that since the nature itself is complex, so should be our theories of nature (Mitchell 2003, p. 115). Like other pluralists she claims the diversity of nature and its phenomena cannot be understood with reductive, monistic theory. In my understanding Mitchell is basing her arguments on observation that functions and structures are usually explained, at least partly, by their evolutionary history and interaction with environment. This implies there is so much variety in their nature that a simple explanation would be unable to understand it.

To support her view, Mitchell notes that the monistic theory[10], or a scientific theory based on idea of unity, does not take into account that when we have multiple different phenotypes of same thing, we cannot give them similar explanation without losing information (Mitchell, 2003, p. 115). Mitchell seems to refer to a notion of reductive scientific unity. The notion of the reductive scientific unity is that various sciences should form a collective theory reducible to a single root science (van Riel & Van Gulick, 2016). Usually this root science is considered to be physics. However, simplified explanations ignore that the interaction of parts pays a significant role in development and structural properties of the whole (Mitchell, 2003, p. 115). Mitchell continues:

> "In short, the multilevel, multicomponent, complex systems that populate the domain of biology are ill suited to a simple, unified picture of scientific theorizing. Pluralism in this domain is not an embarrassment of an immature science, but the mark of a science of complexity." (Mitchell, 2003, p. 115.)

For the etiological view a function is a result of X's existence. Etiological theory is concentrated on explaining why a certain feature occurs. Therefore, we may argue it does not straight forward explain what something is and what kind of description it should be given. Etiological theory gives us an explanation for X being in the world but is this enough for explaining the nature of X? To put it other way, an apple tree's feature of growing apples may well be explained by etiological theory, but is it able to give us the definition on what is an apple?

Etiological theory's challenge remains the question of how we are able to know all the evolutionary events that have played an essential part in the development of the function. When the explanation of function is this much dependable of our knowledge of past, the definition is more open to biases than structural definition. Even tough, the

[10] Monistic, microstructural theory, as introduced by Hendry(2006) and Brid & Tobin (2017).

structural definition is dependable of our current ability to research the structure of the subject, it seems to be less open to false understanding than examining the past.

Mitchell cites Millikan asserting that since the function of a subject is determined by its history, defective individuals do not cause problems for etiological theory (Millikan, 1984, p. 17; Mitchell, 1995. p. 45). Individuals of same class have a shared causal history and therefore they can be categorized into a same kind even if the functions do not actualize.

## 7.2 Monarch butterfly and Viceroy butterfly: functions and mimesis

Instead of using imaginary thought experiments[11] to examine problems of etiology, Mitchell suggests we should turn to look for real life examples. She claims the fictive examples are problematic as they create unnecessary complications and do not necessarily meet the requirements of the real world (Mitchell, 1995, p. 45). She adds that examining the biological world we can find examples better suitable for the purpose of philosophical research. Furthermore, real life examples are easier to integrate to the practical demands of research than the classic examples (Mitchell, 1995, p. 45).

Mitchell finds a promising real life example from the phylum of *Arthropoda* (Mitchell, 1995, pp. 45–46). A Monarch butterfly and Viceroy butterfly are both butterflies living in the same areas of North America, Mexico and Canada. Both species share similar coloring patterns, but the background of the colorization is different. Monarch butterfly's coloring serves as a warning sing for predators. The caterpillars feed on

[11] Such as a thought experiment about two identical worlds, introduced by Bigelow and Pargetter (see Bigelow & Pargetter, 1987, p. 188; Mitchell, 1995, p. 45)

milkweeds and due to this diet, the crown up Monarch butterflies are toxic with cardiac glycoside and most predators avoid catching Monarchs once tasted them. Viceroy butterflies on the other hand are suitable food source for predators, but because their coloring resembles that of Monarch, they, too, avoid predators; after a bird has tasted Monarch butterfly it avoids also catching Viceroy butterflies that resemble Monarchs. This kind of advantageous resemblance is called “mimicry” and is one form of directional selection.

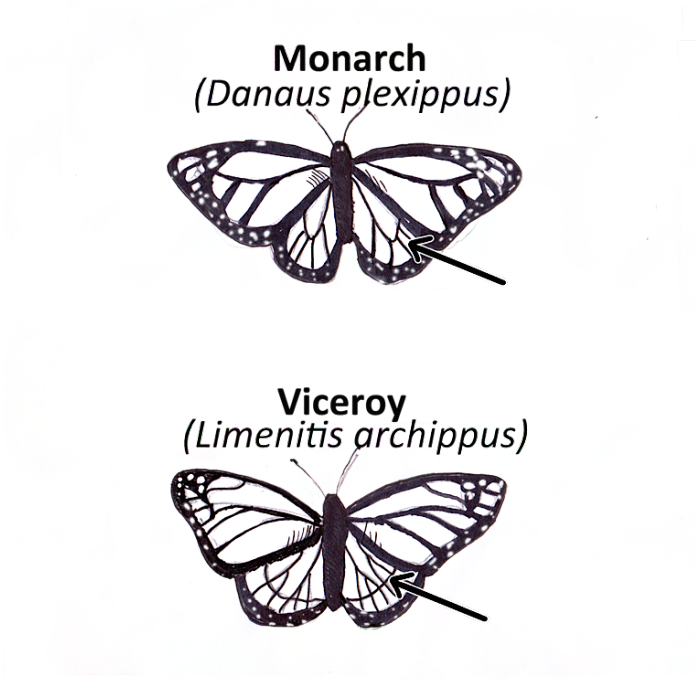


**Figure 3: Differences between Monarch and Viceroy butterflies.[12]**

[12] Own work.

Though Monarchs and Viceroys are structurally similar to the extent that predators are unable to distinguish them, Mitchell claims the mimics and models do not have the same function (Mitchell, 1995, p. 47). While the function for the colorization of Monarch is to warn predators, "mimetic characters have been evolved for a specific mimetic function" (Mitchell, 1995, p. 47). Therefore, from an etiological point of view colorizations do not have the same functions since they do not share the same evolutionary history and background. Mitchell explains:

> "The function of the conspicuous coloration in the Monarch is to warn the predator of its unpalatability. The function of the Viceroy coloration is to mimic the model and deceive the predator into presuming it is unpalatable and thereby avoid predation." (Mitchell, 1995, p. 47)

Without knowledge of the evolutionary background the difference of the functions is not obvious. Indeed, it may well be thought that the similar colorizations have the same functions. The knowledge on causal, evolutionary history enables us to do these distinctions. (Mitchell, 1995, p. 47.) Of course, we may suggest both colorings serve function of survival by avoiding predators. However, this seems to ignore crucial differences between functions. We may elaborate this with an example of two persons with shotguns. Both persons hold a gun on their right hand and a warning sign on their left hand. The sign says they will shoot if under threat. However, while the person A has a loaded gun with bullets, the person B has merely a toy gun that greatly resembles a real one. Both, A and B, can use their guns to stop an attacker C. However, only person A's gun can actually do what the warning sign says. Do the signs held by A and B share the same function? It seems not. Eventhough they both signs serve as a tool for survival, A's sign refers to an actual potantial outcome, while B's sign does not. Their functions are not completely different, but they are not the same because *the guns that signs refer to*, are not the same kind.

Viewing functions of proteins in the light of Mitchell's example, it becomes evident the functions alone cannot define proteins. Functions, dispositions and etiological theory

can provide us an explanation on many important parts of a protein, but they do not give us a description of the microstructure. Even if we agree that etiological theory is able to explain the differences between seemingly similar functions, we are still left without an adequate structural explanation. Of course, we may claim the structural description is not needed, but that would be in contrast with the views of chemical science and biology. If we wish to build a theory that is also in balance with the practices of chemical sciences, it appears the functional explanation alone is not sufficient. Colorization of wings is what it is due to the specific properties of the molecular structure. These structural properties are more or less the same in different butterfly species. This structure-level explanation is not what etiological theory is interested in. That been said, if we examine the case of butterflies and their colorization, microstructural explanation does not seem to be enough either. Microstructural explanation (of the chemical structure) of the wing colorization does not provide us with any explanation or definition on why it seems plausible to claim Monarchs and Viceroys colorizations do not have the same function. Microstructural theory would seem to view them as similar as long as the structural composition is the same. Therefore, strict microstructure cannot fully explain functional properties.

Slater's central idea bears similarities with Mitchell's etiological approach. Slater considers crucial how the function contributes to the survival and development of the organism (Slater, 2009, p. 859). In explaining functions, Slater leans on systemic-capacity approach instead of an etiological explanation. According to Slater the theory aims "to understand the function of a component in terms of its contribution to the capacities of the larger system". (Slater, 2009, p. 859.)

It may be noted, that while Slater's theory is more focused on causality and on future events of an organism, both theories consider the relation of the function, trait and the surrounding organism (or species) important. Functions seem to have properties that get their content from the historical timeline, potential future and from interaction with

surroundings[13], not from the chemical structure. Even more, it seems these functional properties are not reducible to the chemical structure since their nature is more of relational and teleological than structural. This, of course, means that explaining functional aspects with only microstructural theory becomes challenging, that is, unless we are willing to accept Goodwin's microstructuralism or other form of microstructuralism that is able to avoid reducing functions solely to the chemical structure.

## 7.3 Dispositional properties and the structure

Mitchell's butterfly example is appealing in many ways. It does not only offer an example from the sphere of natural sciences but also avoids some of the counter arguments that classic examples have faced. Still it is obvious that the structural properties need to be taken into account as well. Mitchell makes a distinction between dispositional properties and the molecular structure of an object (Mitchell, 1995, p. 49). Both properties can be given as an example for the behavior of the object.

Mitchell offers a property of 'fragility' as an example. According to her, we may explain why an egg breaks by its disposition 'being fragile' or by its specific molecular structure that enables the fragility. The first explanation "abstracts away from the particular material of the causal basis and picks out a class of causally efficacious properties". The latter explanation concentrates on causes than enable "the manifestation in this instance". (Mitchell, 1995, p. 49.)

[13] Depending on the theory of functions the focus between these three may vary.

This may be in the following way: while the property ‘fragility’ *explains* why an object breaks if dropped, the object *is* fragile because of a certain microstructure it possesses. Therefore, functions are based on the microstructure, but the functions are not reducible to it. Similarly, as we can assert that emotions are being made possible due to certain physical structures but reducing emotions solely to the physical structures would overlook other important aspects of what they are.

It is also good to note that while Mitchell makes a distinction between dispositional explanation and etiological explanation, both explaining functions, these theories do not compete. According to Mitchell dispositional theory and etiological theory use ‘function’ differently. While dispositional theory explains the role of currently present function, the etiological theory seeks to explain the reasons why the trait has developed. (Mitchell, 1995, p. 51.)

This interpretation pulls towards the theory offered by Goodwin. According to Goodwin the microstructural properties give the basis for the nature of an object but in addition to this, other explanatory levels are needed. Even though these levels have their basis in the primary structure, they cannot be reduced to it without losing essential aspects of the description. (Goodwin, 2011, pp. 541–544.)

# 8 Conclusions

This thesis has examined some contemporary issues that have caused much debate in the contemporary discussion on macromolecules and their status as natural kinds. It is obvious the answer to the question of which theory we should adopt is hard to give, as all of the theories introduced are struggling with some aspects of protein classification. Nevertheless, if we accept some basic assumptions such as that the theory should be in balance with natural sciences it seems to pull us towards the theories offered by Bartol and Goodwin.

I argue that accepting pluralism would mean biting a bullet. Pluralism does not explain why (microstructural) monism is closer to successfully used methods of scientific practice. In addition to this, as examined chapter 6.2.2., pluralism does not provide us any tidier explanation to all the other problems associated with proteins. Furthermore, pluralism hasn't been able to explain why it so strongly appears the chemical structure of an object is its basic structure. This intuition is supported by the practices of natural scientists and if we wish our theory to remain in balance with current scientific knowledge, microstructure and chemical structure should be considered as the primary definition, or at least important part of the definition of a composition.

If we are ready to jettison the assumption of macromolecules as kinds, we can consider Bartol's view as a good starting point. He considers macromolecules, such as proteins, to be both biological and natural kinds. Therefore, proteins are essentially two different kinds, biological and chemical, and they should be treated as such. Practical implications for adopting Bartol's view could be that whenever classifying and examining proteins the functional and structural properties should have as much importance. According to Bartol's view microstructural properties are not in any way more fundamental and they should not be treated as such. Proteins are what they are by virtue of their biological properties and their chemical structure.

Goodwin offers us a promising way to develop microstructuralism (Goodwin, 2011). By adding additional explanatory levels, the problems of microstructuralism can be fixed without accepting pluralism or Bartol's dualism of kinds. This kind of revision should not be reviewed as an ad hoc change but well grounded development of the theory. That been said, strict distinction between functions and chemical structure, as well as between monism and pluralism, creates an unfruitful ground to build a theory. Explaining versatile world needs theories that do not simplify too much of the knowledge. However, to accept too versatile explanation does not do any better. Therefore, theories capable to explain natural kinds without leaving essential information out while being compatible with current scientific research are the most promising starting ground. With that in mind, as stated earlier, metaphysical and philosophical research should not be subordinated to the limits of scientific practice as their goals differ. While the latter leans on empirical studies, philosophical research seeks also the argumentative basis of the objects of research (Bartol, 2016, p. 548).

I suggest that if we wish to hold on to the idea of macromolecules as natural kinds, the most appealing theory is the one offered by Goodwin. His leveled monism offers a possibility to hold on to natural kind monism and yet to be able to give them a description that explains also functions that have caused problems to strict monism. As Goodwin's theory considers microstructural properties most constitutive, it does not fall into pluralism. Instead the other explanatory levels are like cream on a cake, they are important part of what the cake is, but the grounding explanation remains microstructural.

It is very likely that future microbiological research will provides us more information about the structure and functions of proteins. However, since the questions set by microbiologists and philosophers differ not only by their form but also by their aim, philosophical enquiry does not need to wait these scientific findings to be able to clarify the classificatory obscurity of proteins. I hope this thesis has proved that the problems

with defining proteins and their essence are of philosophical nature and therefore can be examined by philosophical means. However, the scientific practice should also be taken into account and knowledge gained from the fields of chemistry and biosciences should not be ignored. Like Tobin argues (2010b), the current hierarchical taxonomy practices as well as the concepts of natural kinds have trouble in adapting to the functionally diverse macromolecules. This means that the theories need to be able to develop. Of course, this is what philosophy essentially is. Our philosophical understanding of the world has to be flexible enough to be able to evolve as we gain new knowledge.

Perhaps the search for an adequate definition can be best described with an analogy: Searching a neat reductive explanation for complex objects with structural and functional properties is like removing from a human everything else but the skeleton and to assert the skeleton is what a human is. However, for a proper description various different traits and structural properties are needed to take into account. By jettisoning them as irrelevant might leave us with nothing but a skeleton. And even more, it makes understanding of any new, various functions difficult, as there is not enough left in the description to explain them. “To carve nature to its joints” should therefore not mean that the flesh is carved away in order to find the true nature. Perhaps a better phrase comes from a surprising source. In J.R.R. Tolkien’s *The Lord of the Rings: The Fellowship of the Ring* wizard Gandalf wisely states to Saruman, another wizard: “He that breaks a thing to find out what it is has left the path of wisdom”(Tolkien, 2005).

Therefore, we might have to accept that, rather unsatisfying, fact that proper definition of a natural kind, such as protein, is built on more than just a straightforward reduction. However, this does not mean accepting pluralism. We may follow Bartol and deny that there is a different class of natural kinds such as “biochemical kinds” and instead suggest that biochemical objects always belong to two classes of kinds; biological kinds and chemical kinds (Bartol, 2016, p. 549). We may also follow Goodwin in suggesting that

the monistic view can be revised into leveled monism, where there are macromolecular kinds, defined not only by their microstructure but also by other levels of properties that support the description.

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